Published Quarterly in October, January, April and July

Entered at New York Post Office as Second Class Matter.

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JOURNAL OF ANATOMY

(ORIGINALLY THE JOURNAL OF ANATOMY AND PHYSIOLOGY)

CONDUCTED, ON BEHALF OF THE ANATOMICAL SOCIETY OF GREAT BRITAIN AND IRELAND, BY

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VOL. LI.

PART III.

APRIL 1917

LONDON: CHARLES GRIFFIN AND COMPANY, LIMITED, EXETER STREET, STRAND 1917

Annual Subscription, 21s. post free.

BIOMETRIKA

A Journal for the Statistical Study of Biological Problems

Founded by W. F. R. WELDON, FRANCIS GALTON and KARL PEARSON. Edited by KARL PEARSON

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JOURNAL OF ANATOMY

THE DEVELOPMENT OF THE HYPOPHYSIS CEREBRI, PRE-ORAL GUT, AND RELATED STRUCTURES IN THE MARSUPIALIA.

By KATHARINE M. PARKER, B.Sc. (Lond.), *Assistant in the Department of Zoology, University of London, University College.*[1]

INTRODUCTION.

THE following investigation of the development of the hypophysis cerebri in Marsupials was undertaken at the suggestion of Professor J. P. Hill, and I wish to express my gratitude to him for help and advice without which the work would have been impossible.

The literature of the pituitary is already vast, and for close on a century its origin has been the subject of much scientific discussion, but relatively little work has been done on the later stages of its development. The rich supply of embryological material in Professor Hill's collection makes it possible to add some facts to those already recorded by other authors, whilst the interesting conditions revealed in some of the Marsupials afford a further reason for adding this contribution to the existing literature.

The pre-oral gut (Seessel's pocket) in some Marsupials actually becomes part of the so-called anterior lobe of the pituitary, hence it becomes necessary to include as full an account as possible of that structure. Furthermore, the relations of the anterior end of the notochord to Seessel's pocket are, in some species, so close as to merit description in the same connection; whilst in intimate relation to the anterior end of the chorda there is, in some Marsupials, a mass of cells giving rise to a pair of head cavities. In fact, study of the region of the head shows that the notochord, head cavities, pre-oral gut, and the hypophysis are so closely related that to omit any one of these structures is to render the description inadequate. It is doubtless impossible at present to arrive at a correct estimation of the phylogenetic importance of the facts, and further study on the subject, more especially in the

[1] Thesis approved for the Degree of Doctor of Science in the University of London.

lower Vertebrates, is very desirable. The difficulty of the problem is evident from the number of different structures of unknown significance which are said to be derived from either the roof of the fore-gut or the head of the notochord—*e.g.* the "præchordal Platte" described by Oppel (40) in *Anguis fragilis*; the "Gaumentasche" of Selenka (55) in Didelphys; the pharyngeal bursa, first described by Mayer (31) in 1840, whose possible identity with Seessel's pocket has since been discussed. From an investigation based on one sub-class of the Vertebrates it is obviously impossible to deduce theories of general applicability, but, at the least, some facts may be added which will in the future help in the solution of the interesting problem of the phylogeny of the Vertebrate head.

The descriptive portion of the paper is divided into two sections: the first dealing with early stages in which the relations of the notochord, fore-gut, oral plate, and hypophysis can be studied; the second, with the process of conversion of the simple evagination of the oral ectoderm into the glandular portion of the adult hypophysis. I have referred only briefly to some phases through which the infundibular process passes, and have deliberately omitted any description of the development of the portion of the diencephalic floor lying in proximity to the pituitary body. During preservation the brain is very apt to become abnormally folded, and the infundibular process is undoubtedly distorted in several of the embryos which have come under my observation. On the other hand, it is difficult to give a satisfactory description of this region of the brain from study of transverse series without making reconstructions. As I hope in the future to work out the development of the fore-brain in Marsupials, which will involve making models of several stages, I propose to deal with the diencephalic floor in a later paper, and it is probable that some further facts may then be added to the present description of the development of the infundibular process itself.

I wish to thank Mr F. C. Pittock, of University College, for much help, both in the making of a model and in various other ways.

Description of Stages.

Section I.—*Early Development of the Chorda, Fore-gut, Premandibular Somites, and Hypophysis.*

Before passing on to stages immediately prior to the formation of the hypophysis, it will be well to briefly review the relations of chorda and fore-gut which are brought about on formation of the head-fold.

From the very complete series of early stages of Perameles in Professor Hill's collection, it is possible to work out the early history of the fore-gut

and chorda in considerable detail. It is not within the scope of the present paper to deal with this subject except in so far as it sheds light on the early relations of the oral plate, gut, and notochord. Perameles possesses a very well-marked protochordal plate (*cf.* figs. 69 and 71 in Wilson and Hill's "Observations on the Development of Ornithorhynchus" (63)), which, like the chorda itself in early stages, is continuous laterally with the entoderm of the gut. When the head-fold forms, this protochordal plate is involved therein and forms the wall of the anterior extremity of the fore-gut. During this period the entoderm closes in below the notochord, which accordingly becomes detached as a solid rod of cells. The protochordal plate, on the other hand, retains its original relations to the entoderm on either side of it, and continues to form the actual wall of the anterior angle of the fore-gut. Its originally anterior portion, which on formation of the head-fold becomes ventral, constitutes the entodermal layer of the oral plate.

STAGE I. *Perameles nasuta* (2 P.). — Fig. 1 represents a median longitudinal section through an embryo of *Perameles nasuta* (2 P.), the drawing being made by reconstruction from several sections near the middle line. The brain, which is as yet open except in the region posterior to the auditory neuromere, is flexed at two points, representing the dien-mesen (D.-M.) and the mesen-metencephalic (M.-Mt.) limits. Posterior to the projecting anterior border of the medullary plate is a rounded depression, the primitive infundibular recess (I.).

The gut has attained a considerable size in the dorsi-ventral direction. Its anterior wall is in intimate contact with the brain, while the anterior portion of its ventral wall forms, with the ectoderm, the oral plate (O.P.). These two portions of the gut wall, which are derived from the protochordal plate, consist of cells which are rich in protoplasm and contain a number of darkly staining granules (Pt.P.). This appearance is characteristic of the protochordal plate of earlier stages. The dorsal wall of the fore-gut consists of cubical or columnar cells with little protoplasm. Posterior to the region shown in the figure, the gut wall consists of much-flattened entoderm cells.

The notochord in the trunk region is small and typical, but becomes slightly thickened in the region of the myelencephalon (Ch.), whilst immediately posterior to the second point of flexure of the brain it passes into a dense mass of cells (P.P.) extending forwards and tapering in front of the anterior flexure to a fine point. This tapering extremity is so intimately connected with the wall of the fore-gut that the two structures are here indistinguishable, and their point of fusion represents in this stage the posterior limit of the protochordal plate.

In transverse section (fig. 2) it is seen that this mass of cells (P.P.) is narrow from side to side, while from its anterior extremity there arise a small pair of solid outgrowths (Pm.S.). (*N.B.*—Only one of these is shown completely in the figure, as the sectional plane is slightly oblique.)

In a prior stage of Perameles, represented by a flat embryo, the slender notochord is directly continuous at its anterior end with the protochordal

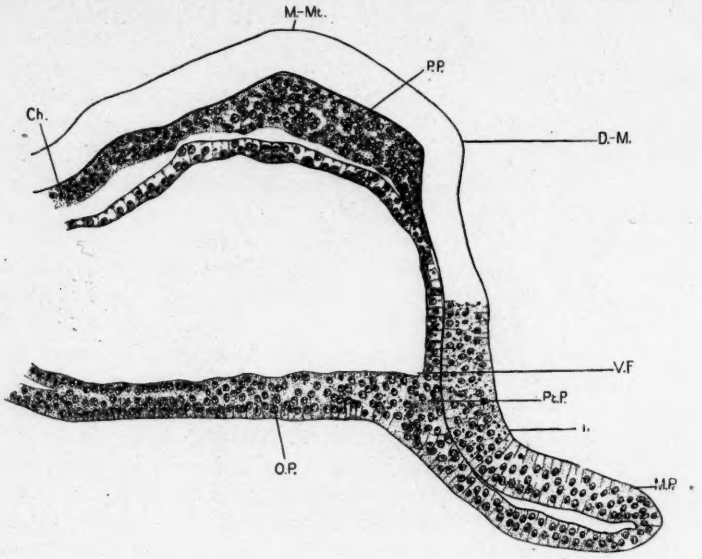

FIG. 1.—Stage I. *Perameles nasuta* (2 P.). Median longitudinal section (reconstructed).

Ch., chorda; D.-M., dien-mesencephalic limit; I., primitive infundibular recess; M.-Mt., mesen-metencephalic limit; M.P., medullary plate; O.P., oral plate; P.P., prechordal plate; Pt.P., protochordal plate; V.F., ventral angle of fore-gut.

plate, and no such mass of cells is present. From its position and relations it is clear that it represents that mass of tissue connecting the gut and notochord which has been described by Oppel (40), Platt (43), and others, in lower Vertebrates; and this lends support to the view that the small outgrowths represent the first trace of the premandibular somites. As we shall see, these structures are clearly present in embryos of *Bettongia gaimardi* and *Macropus ruficollis* of a slightly later stage. Moreover, though it is impossible to trace their history continuously, we find undoubted premandibular head-cavities in the next stage of Perameles, the

subsequent history of which has already been described by Elizabeth A. Fraser (12) in Professor Hill's material.

We may therefore conclude that the mass of cells at the anterior end of the chorda represents the "præchordal Platte" of Oppel, and that its lateral outgrowths are the rudiments of premandibular head cavities. I shall accordingly refer to the cell mass in question as the prechordal plate.

There is no differentiation of hypophysial epithelium at this stage.

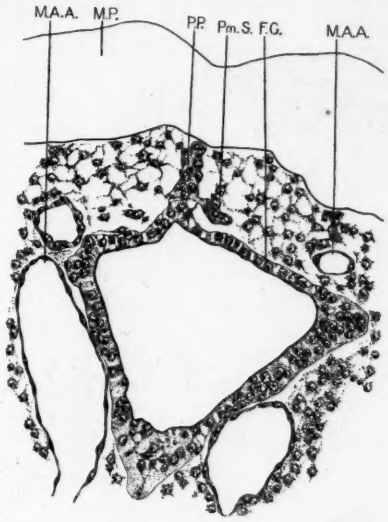

FIG. 2.—Stage I. *Perameles nasuta* (2 P.). Transverse section through prechordal plate and rudimentary premandibular somites. Sl. 1-3-4.

F.G., fore-gut; M.A.A., 1st (mandibular) aortic arch; M.P., medullary plate; P.P., prechordal plate; Pm.S., premandibular somite.

STAGE II. *Bettongia gaimardi*.—This embryo is at a slightly later stage than that of *Perameles nasuta* (2 P.), Stage I., described above, but in the relations of the brain, gut and notochord there is very close agreement between the two embryos.

The brain is flexed at two points, the hind-brain is closed, while the mid- and fore-brains are still widely open.

The anterior wall of the fore-gut lies against the floor of the fore-brain and forms a well-marked angle with the roof. It is somewhat thickened, and is presumably derived from a protochordal plate as in Perameles.

At the anterior end of the notochord is a thickened mass of cells which is bent over so that its anterior extremity lies between the floor of the fore-

brain and the anterior wall of the fore-gut, while the apex of the bend lies above the antero-dorsal angle of the gut. This mass of cells represents the prechordal plate of Perameles, but is less well-marked, and, although its anterior extremity is in close contact with the wall of the fore-gut, there does not appear to be actual continuity between the two structures at this stage.

On each side of the embryo, lying posterior to the well-developed optic

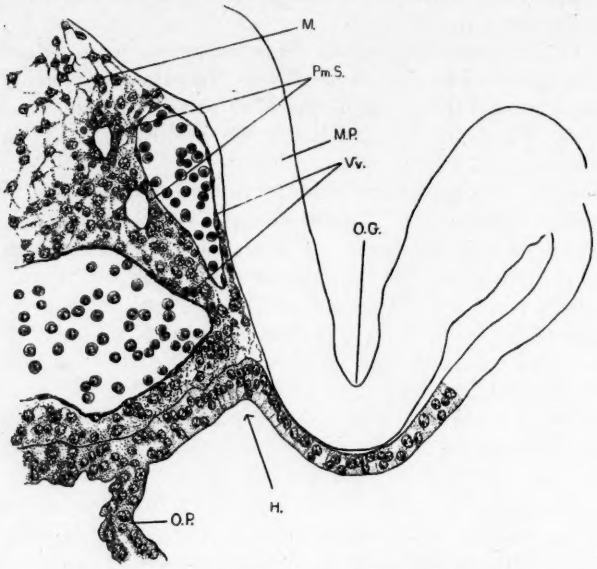

FIG. 3.—Stage II. *Bettongia gaimardi.* Longitudinal section passing through the optic groove and premandibular somites. Sl. 2–2–2.

H., hypophysial angle; M., mesenchyme; M.P., medullary plate; O.G., optic groove; O.P., oral plate; Pm.S., premandibular somite; Vv., blood-vessels.

groove (fig. 3, O.G.), there is a mesodermal mass which can readily be distinguished by its relative density from the loose mesenchyme of the head (fig. 3, Pm.S.). Furthermore, each of these mesodermal masses contains several small but perfectly distinct cavities, two of which are shown in fig. 3, round which the cells are arranged in a radiating manner, forming an irregular epithelial wall. These cavities are not symmetrical on the two sides of the embryo. Owing to the fact that the head of the embryo is cut longitudinally, it is very difficult to determine the exact lateral and median limits of these structures, but after careful study of the series, I

have been able to make out that a fine strand of cells connects each mass with the anterior end of the prechordal plate. From the position and relations of these structures it is evident that they represent premandibular somites. The fact that more than one cavity is present in each mesodermal mass does not appear to indicate the presence of more than one pair of somites, for the cavities are irregularly arranged and are not symmetrical on the two sides of the embryo.

The hypophysial angle (H.) is recognisable, but there is no differentiation of the ectoderm in this region.

STAGE III. *Macropus ruficollis.*—This embryo shows a distinct advance on the Bettongia embryo described above. The brain is sharply flexed at the mesen-metencephalic junction, the hind-brain is closed, the mid-brain widely open, whilst in the fore-brain the medullary folds are closely opposed but not yet fused.

The fore-gut, in correlation with the flexure of the brain, has a well-marked antero-dorsal angle. Its anterior wall is not thickened as is the case in Perameles and Bettongia. The notochord is discontinuous in the region of the hind-brain. At its anterior end, which still persists, there is a slight enlargement, bent at an acute angle and lying between the antero-dorsal angle of the fore-gut and the floor of the mesencephalon at the point of flexure. This structure, the reduced remnant of a prechordal plate, is not in actual continuity with the wall of the fore-gut.

On each side of the fore-brain, postero-lateral to the optic vesicles, there is a group of mesoderm cells,[1] similar to those described in the same situation in *Bettongia gaimardi* (fig. 4, Pm.S.).

Each cell group is distinguishable from the surrounding mesenchyme by its relative density, and contains several small cavities around which the cells are arranged in the form of a fairly definite epithelium (Ep.H.C.). The two masses are connected across in the middle line by a transverse "bridge" (B.) consisting of a fine, solid strand of cells which runs across immediately anterior to the tip of the notochord.

The sectional plane of this series is transverse to the notochord, and the existence of the bridge is accordingly perfectly clear. On the other hand, it is very difficult to determine whether or no the tip of the prechordal plate is in contact with the bridge connecting the somitic masses. As, however, the section showing the connecting piece is next to that in which the tip of the notochord is seen, it is clear that they are at least in very close proximity to each other.

The mesodermal masses of this embryo bear to the notochord and gut

[1] My attention was first drawn to the presence of these structures in this embryo by Professor Hill.

the relations which characterise premandibular head cavities, which we may accordingly assume them to be.

The ectoderm of the head is unmodified at the base of the oral plate, *i.e.* there is as yet no differentiation of the hypophysial epithelium.

Trichosurus vulpecula.—This stage is represented in the Trichosurus series by two embryos, one cut longitudinally, the other transversely. These embryos show a very close resemblance to that of *Perameles nasuta* (2 P.), Stage I., in the relations of gut, brain, and notochord, but in several respects they belong more properly to the same stage as the Macropus embryo described above. As they show nothing new, it is not necessary to give a separate description of them, but it may be noted that structures

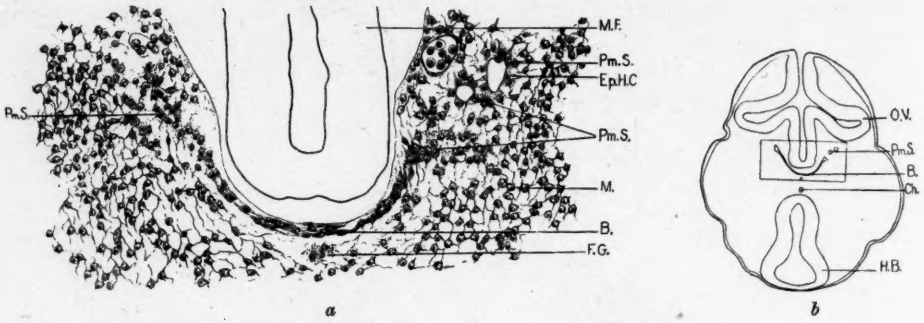

FIG. 4.—Stage III. *Macropus ruficollis.* (*a*) Transverse section through premandibular somites; (*b*) outline diagram of whole section of which (*a*) is a part. Sl. 1–4–5.

B., bridge connecting premandibular somites; Ch., chorda; Ep.H.C., epithelium of head cavity; F.G., wall of fore-gut; H.B., hind-brain; M., mesenchyme; M.F., medullary fold; Pm.S., premandibular somite; O.V., optic vesicle.

similar to the undoubted head cavities of *Macropus ruficollis* are present in one of the embryos of Trichosurus at this stage of development.

STAGE IV. *Perameles nasuta* (13, VII. 05).—This embryo shows a distinct advance on the preceding, the brain being completely closed and Rathke's pouch already differentiated. It is cut in horizontal sections, and, as the relations of the parts are particularly interesting, a wax plate-reconstruction was made of the fore-brain, hypophysis, chorda, etc. (see fig. 5). Detailed observations are, moreover, made possible by the remarkably perfect preservation of the embryo.

The floor of the diencephalon shows a rounded depression, the primitive infundibular recess (I.), anterior to which is a slight ridge, indicating the future position of the optic chiasma. The hypophysial primordium—Rathke's pouch (R.P.)—is now present as a thickened stretch of ectoderm,

closely applied to the infundibular depression. The pouch is very shallow anteriorly and deepens somewhat behind, where its lateral angles are fairly well marked. Its posterior wall forms the anterior wall of the fore-gut, and constitutes the ectoderm of the dorsal portion of the oral plate (O.P.), which is still complete. In its dorsal portion, the oral plate is bent at a fairly sharp angle, the apex of this angle forming in section a "plug" (P.) which

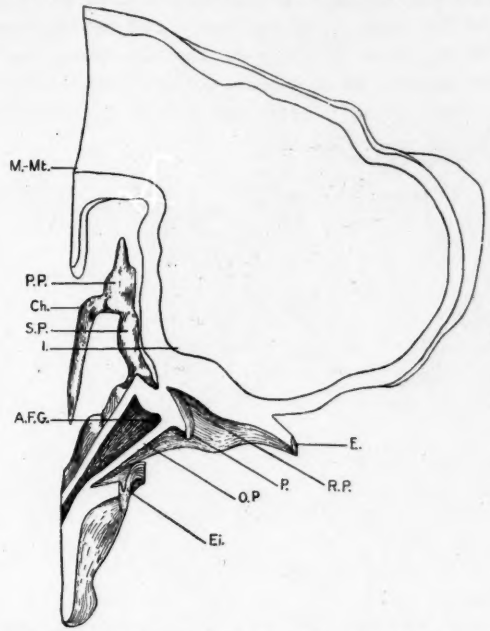

FIG. 5.—Stage IV. *Perameles nasuta* (13, VII. 05). Longitudinal section through model of fore-brain, hypophysis, Seessel's pocket, and notochord, slightly to the right side of the middle line.

A.F.G., anterior angle of fore-gut; Ch., chorda; E., ectoderm of head; E.i., ectoderm of mandibular arch; I., infundibular recess; M.-Mt., Mesen-metencephalic limit; O.P., oral plate; P., "plug" formed by projection of oral plate into Rathke's pouch; P.P., prechordal plate; R.P., Rathke's pouch; S.P., Seessel's pocket.

projects into Rathke's pouch, and will be seen in similar stages in other species (*cf.* fig. 31, O.P.), whilst the rest of the oral plate is thin.

The dorsal wall of the fore-gut is thickened immediately behind Rathke's pouch, and from it there arises a small median outgrowth (S.P.), slightly dilated at its extremity and running backwards parallel with the diencephalic floor to meet the somewhat irregular prechordal plate (P.P.). This latter preserves its original form, being narrow from side to side and

of relatively considerable dorso-ventral extent. The prechordal plate is continuous at its caudal extremity with the notochord (Ch.), which is here small and typical, and, following the flexure of the brain, is bent at approximately a right angle at the mesen-metencephalic junction (M.-Mt.).

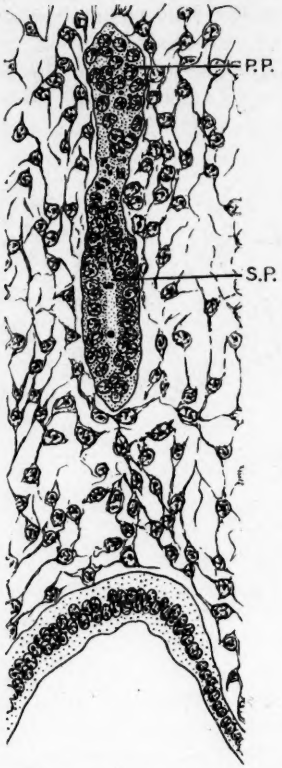

Fig. 6.—Stage IV. *Perameles nasuta* (13, VII. 05). Section through prechordal plate and Seessel's pocket. Sl. 3–3–11.

P.P., prechordal plate; S.P., Seessel's pocket.

The small outgrowth (S.P.), arising as it does immediately behind the oral plate, represents the remnant of the pre-oral gut usually known as Seessel's pocket. It will be noticed that its distal extremity is continuous with the prechordal plate, and we may therefore conclude that it has arisen from that part of the fore-gut of the early stage of Perameles which

is situated at the junction of the prechordal plate with the entoderm of the gut wall.

The minute structure of the organs in this region is also worthy of note. The thickened wall of the fore-gut immediately behind Rathke's pouch shows all the features characteristic of the protochordal plate of earlier stages, the granulation of the cells being recognisable here, and to a less extent in the portion of oral plate adjacent to it. We may therefore conclude that here, as in the previous stage, the antero-ventral wall of the fore-gut is formed by the protochordal plate. Seessel's pocket, arising from the dorsal side of this portion of the gut (fig. 6, S.P.), has no actual lumen

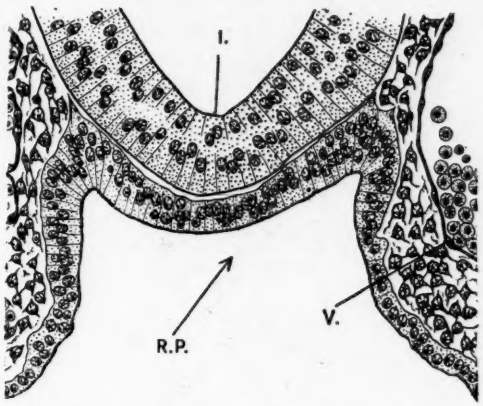

FIG. 7.—Stage IV. *Perameles nasuta* (13, VII. 05). Transverse section through primitive infundibular recess and Rathke's pouch.

I., primitive infundibular recess; R.P., Rathke's pouch; V., blood-vessel.

but is obviously tubular in structure, its walls consisting of a very regular epithelium. It is impossible to define exactly the limit between the wall of Seessel's pocket and the prechordal plate (P.P.), which consists of a rather irregular mass of cells, containing darkly staining granules. From its margin, cells here and there project, giving it an irregular outline, in which respect it contrasts with the notochord proper, whose outline is perfectly definite. Some of these cells appear to represent traces of the former connection between the prechordal plate and the premandibular somites, which have now acquired a considerable size and possess a distinct cavity. In this stage they have already been described and figured by Fraser (12).

The walls of Rathke's pouch (fig. 7, R.P.) consist of a regular columnar epithelium which is thin in the middle line and thickens somewhat at the

lateral angles, where the cells are closely packed and show evidence of rapid growth. Thus there is a tendency for the cells in these two regions to project on the outer side of the wall, giving almost an appearance of proliferation (fig. 7), a condition which is doubtless due to the rapid multiplication of the cells.

Dasyurus viverrinus.—As Dasyurus differs in some important respects from the types described above, and as, moreover, a complete series of stages showing the early development of Rathke's pouch is available, it will be best to describe the stages of Dasyurus consecutively as a series, distinct from Perameles, Bettongia, and Macropus.

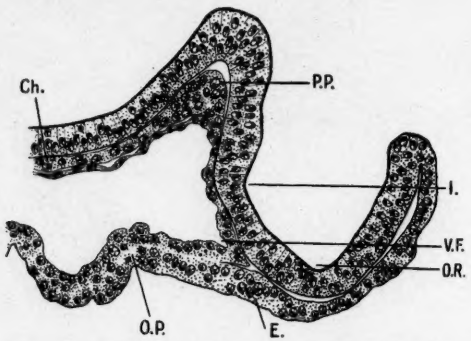

FIG. 8.—Stage I. *Dasyurus viverrinus* (I., A. 02). Median longitudinal section through the anterior end of the brain, chorda, and fore-gut (reconstructed). Sl. IV. 1–14 to 2–1.

Ch., chorda; E., ectoderm; I., primitive infundibular recess; O.P., oral plate; O.R., optic recess; P.P., prechordal plate; V.F., ventral angle of fore-gut.

STAGE I. (I., A. 02).—This stage corresponds approximately with Stage I. of Perameles.

The relations of brain, gut, chorda, and oral plate are best seen in median longitudinal section (fig. 8). The brain is flexed at one point, while the hind-brain only is closed. The anterior end of the medullary plate curves upwards, and two depressions in the floor of the fore-brain can be identified. Of these, the anterior is the optic (O.R.), the posterior the infundibular recess (I.). The chorda (Ch.) extends to shortly behind the point of flexure of the brain. Throughout the greater part of its length it consists of a thin strand of cells, but at its anterior end, which lies in the angle formed by the cranial flexure, there is a marked thickening, the prechordal plate (P.P.) bent at an acute angle and reaching its greatest thickness opposite the flexure of the brain floor. The tapering extremity of the prechordal plate, as in Perameles, is directly continuous

with the gut-wall. The antero-dorsal angle of the gut is thin-walled while its antero-ventral angle has relatively thick walls, consisting of somewhat irregular, elongated cells. Here again the whole of the anterior wall of the fore-gut as well as the anterior part of the entoderm of the oral plate is to be regarded as derived, as in Perameles, from a protochordal plate. The latter, however, is not nearly so clearly differentiated in Dasyurus as it is in Perameles.

No traces of premandibular somites are recognisable.

The ectoderm of the hypophysial angle (E.) consists of columnar epithelium, and as yet shows no sign of differentiation.

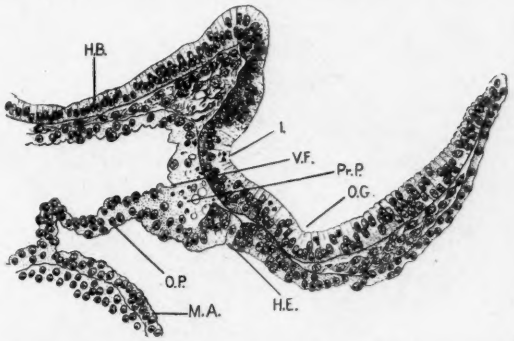

FIG. 9.—Stage II. *Dasyurus viverrinus* (1, 01). Median longitudinal section through anterior end of brain and fore-gut. Sl. 3–3–2.

H.B., hind-brain; H.E., hypophysial epithelium; I., primitive infundibular recess; M.A., mandibular arch; O.G., optic groove; O.P., oral plate; Pr.P., protochordal plate; V.F., ventral angle of fore-gut.

STAGE II. *Dasyurus viverrinus* (1, 01).—In general features this stage resembles the preceding so closely that no detailed description will be necessary.

The brain in median longitudinal section (fig. 9) presents much the same features as in Stage I., but the infundibular depression (I.) and the optic recess (O.G.) are both more clearly defined. The prechordal plate is no longer recognisable as a distinct structure. The wall of the antero-ventral angle of the fore-gut (protochordal plate, fig. 9, Pr.P.) is now distinctly thickened and has a very characteristic appearance. The cells are regularly arranged, contain a number of darkly staining granules, and are vacuolated.

The first trace of the primordium of the hypophysis is now recognisable. Immediately anterior to the oral plate, the ectoderm consists of distinctly elongated epithelial cells (H.E.) The thickening extends forwards as far

as the optic recess, and is most marked at the point of contact of the ectoderm with the entoderm of the pre-oral gut. Posterior to this point the modified ectoderm of the hypophysis thins out slightly and is directly continuous with the oral plate (O.P.), in which the ectoderm and entoderm are now indistinguishable.

In transverse section we can see the primordium of the hypophysis as a thickened and slightly invaginated stretch of ectoderm, in intimate contact with the floor of the brain.

STAGE III. *Dasyurus viverrinus* (II., *a*, 01): *Embryos a, b, and c.*—

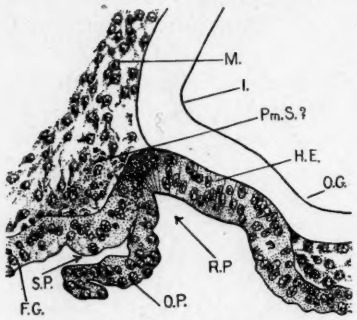

FIG. 10.—Stage III. *Dasyurus viverrinus* (II., *a*, 01). Embryo *a*. Median longitudinal section through the hypophysis and Seessel's pocket. Sl. 2–3–7.

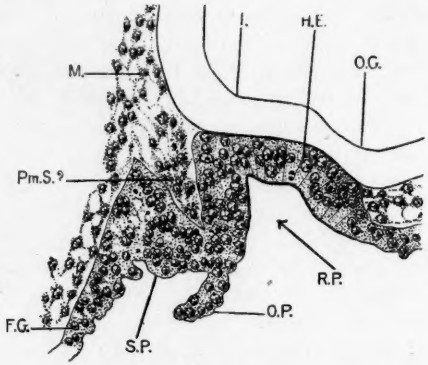

FIG. 11.—Stage III. *Dasyurus viverrinus* (II., *a*, 01). Embryo *c*. Median longitudinal section through the hypophysis and Seessel's pocket. Sl. 2–1–11.

F.G., fore-gut; H.E., hypophysial epithelium; I., primitive infundibular recess; M., mesenchyme; O.G., optic groove; O.P., oral plate; Pm.S.(?), possible trace of premandibular somite; R.P., Rathke's pouch; S.P., Seessel's pocket.

The embryos of this stage are only slightly more advanced than those of the preceding. The optic groove (fig. 10, O.G.) and the infundibular recess (I.) are slightly more clearly marked. The hypophysis has distinctly deepened and the oral plate has ruptured. The relations to the pre-oral gut in individual embryos of the stage vary slightly (*cf.* figs. 10 and 11).

In two embryos (*a* and *b*, fig. 10), which are cut longitudinally, the hypophysis is separated from the anterior angle of the gut simply by the thickness of the oral plate, which is ruptured ventrally (O.P.). The wall of the hypophysis consists of columnar epithelial cells, very regularly arranged. The pouch (R.P.) shows an obtuse anterior angle and an acute posterior angle, and the latter has progressed back so as to lie beneath the deepest part of the infundibular recess. The regular columnar

epithelium extends over the apex of the posterior angle of the pouch and passes into continuity with the thickened wall of the anterior angle of the fore-gut, as well as with the persisting upper part of the oral plate. Seessel's pocket is represented simply by the thick-walled anterior angle of the fore-gut, and is separated from Rathke's pouch merely by the persisting upper part of the oral plate.

In a third embryo (*c*, fig. 11), cut longitudinally, Rathke's pouch is somewhat larger. Moreover, instead of the posterior wall of the hypophysis being in direct contact with the anterior wall of the fore-gut, a certain amount of mesenchyme is present immediately behind Rathke's pouch. Seessel's pocket accordingly forms a small conical diverticulum whose wall is separated from that of Rathke's pouch by mesoderm. The remnant of oral plate (O.P.) is attached to the ventral border of the fold between Seessel's pocket and the hypophysis.

This condition resembles the typical arrangement in many Eutheria and birds, in both of which groups the pre-oral gut forms a short diverticulum separated from the hypophysis by a solid fold containing a mesodermal core.

In all the embryos of this stage there is on either side of the middle line, immediately posterior to the hypophysis, a group of cells lying dorsal to the gut-wall. In the first of the types described above, these cells lie posterior to the apex of the anterior angle of the fore-gut (fig. 10, Pm.S. ?); in the second, they lie between the hypophysis and Seessel's pocket (fig. 11, Pm.S. ?). This cell mass can be distinguished from the surrounding mesoderm by its density and by the presence of a number of darkly staining granules. It seems possible that it represents a pair of somites, presumably premandibular, but apart from it no trace of head cavities has been found in Dasyurus.

Stage IV. *Dasyurus viverrinus* (*β*).—In this stage the floor of the infundibulum is marked by a distinct angle, but no definite infundibular process has appeared.

The hypophysis now forms a distinct pouch, with a small remnant of the oral plate attached to its posterior wall in some embryos. In one embryo only of this stage is there still a considerable remnant of Seessel's pocket; in the others, a very slight diverticulum (fig. 12, S.P.) marks the position of the pre-oral gut; but in every case the posterior wall of the hypophysis, though continuous with, is perfectly distinct from, the anterior wall of Seessel's pocket.

It is evident from the foregoing that in Dasyurus, Seessel's pocket is a variable and transient structure, for it is hardly recognisable in some embryos, and in no case does it play any part in later development.

It has not been possible to recognise in this stage the group of cells described in the preceding stage and interpreted as possibly somitic.

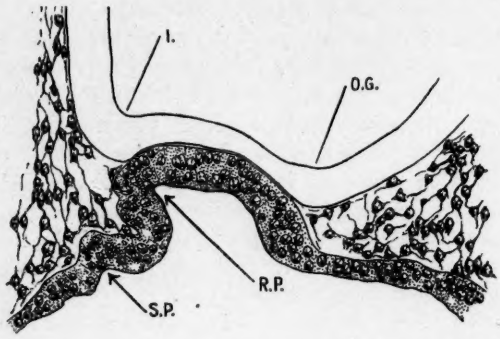

FIG. 12.—Stage IV. *Dasyurus viverrinus* (β). Median longitudinal section through hypophysis. Sl. 2–6–11.

I., primitive infundibular recess; O.G., optic groove; R.P., Rathke's pouch; S.P., Seessel's pocket.

SECTION II.—*The Later Development of the Hypophysis cerebri and the Pre-oral Gut.*

This section deals with the development of the hypophysis subsequent to the establishment of Rathke's pouch, *i.e.* with the origin and development of the infundibular process and the conversion of the simple buccal invagination into the so-called anterior lobe and pars intermedia of the adult.

With regard to the nomenclature of the parts of the adult hypophysis, it has already been pointed out by Tilney (58) and others that the terms "anterior" and "posterior lobes" and "pars intermedia" are open to serious criticism. They are applicable to the human subject, but not to all Vertebrates, inasmuch as the infundibular process is frequently dorsal to the rest of the pituitary and in some species is actually anterior thereto. Moreover, these terms are based exclusively on topography, and indicate neither the function nor the origin of the parts, for the "pars intermedia" is only intermediate in position and not in any other sense. Furthermore, there is good reason to suppose that the tissue of the non-nervous portion of the hypophysis which is in contact with the nervous portion consists of two parts. As these two regions have been clearly recognised, as far as I am aware, only by Tilney (59), the simplest method is to adopt the

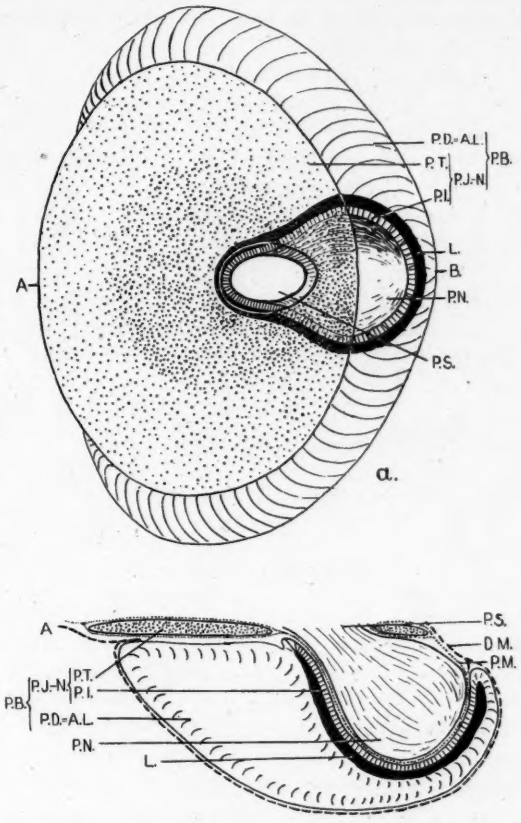

FIG. 13.—(*a*) Diagrammatic ground plan of hypophysis to show the relations of the various parts. The hypophysis is represented as removed from the brain and viewed from the dorsal surface in optical section. (*b*) Diagrammatic median longitudinal section through adult hypophysis. (Sectional plane indicated by line A B in fig. *a*.) (*N.B.*—The relations and approximate proportions of the parts in these figures were obtained by measurement with an ocular micrometer of the hypophysis in *Trichosurus vulpecula*, Stage XI. (see p. 212), H.L. 20 mm., G.L. 4 cm.)

D.M., dura mater; L., lumen; P.M., pia mater; P.S., pituitary stalk;
P.B., pars buccalis; { P.J.-N., pars juxta-neuralis; { P.T., pars tuberalis; P.I., pars infundibularis;
P.D., pars distalis = A.L., anterior lobe;
P.N., pars neuralis.

nomenclature used by him, some of the terms being originally suggested by Gentes (15).

We can accordingly recognise in the hypophysis a *pars neuralis* (fig. 13, P.N.) (=posterior lobe, infundibular process, "Hirnteil," neuro-hypophysis) and a *pars buccalis* (P.B.) (=anterior lobe, epithelial or glandular portion, "Hauptlappen," together with the pars intermedia). The pars buccalis is subdivided into a *pars juxta-neuralis* (P.J.-N.), in contact with the brain, and a *pars distalis* (P.D.) (=anterior lobe proper). The pars juxta-neuralis consists of a *pars tuberalis* (P.T.) (Tilney (59)), lying in contact with the tuber cinereum, and a *pars infundibularis* (P.I.) (=pars intermedia), *i.e.* the epithelial layer between the residual lumen and the infundibular process. The difference in origin and appearance of these two portions of the pars juxta-neuralis which Tilney (59) describes in the fowl, cat, rabbit, rat, and sheep, is also recognisable in Marsupials.

In early stages the use of topographical terms is necessary, and I accordingly describe the parts of Rathke's pouch as dorsal, *i.e.* on the side next the diencephalic floor; ventral, *i.e.* on the side next the pharyngeal roof; cranial, towards the telencephalon; and caudal, towards the mesencephalon.

Trichosurus vulpecula.

Stage I. *Embryos* ♀ 99, 1.01, *and* ♂ 97.—The hypophysis of these embryos shows only a slight advance on that of Stage IV., *Perameles nasuta* (13, VII. 05).

The oral plate is ruptured (fig. 14, O.P.), but its ventral point of attachment is still visible, whilst dorsally a considerable remnant of it persists. Behind the oral plate is a small conical diverticulum with thickened walls. This is the only trace of pre-oral gut which occurs in Trichosurus (fig. 14, S.P.).

On the cephalic side of the oral plate the ectoderm of the head is thickened for a short distance, forming with the ectoderm of the upper margin of the oral plate the primordium of Rathke's pouch (R.P.). Transverse sections show that in its cephalic portion the pouch is widely open on its ventral side, while its dorsal wall is closely applied to the diencephalic floor. The pouch is, however, closed in its posterior portion and is bifid at its caudal extremity. The small pre-oral gut fits into the bifurcation of the pouch so that in the middle line its entoderm is in contact with the floor of the diencephalon, whilst on either side it is separated therefrom by the lateral branches of Rathke's pouch. The wall of the pouch consists of several layers of columnar cells.

The floor of the diencephalon is depressed to form the primitive infundibular recess, whose dorsal limit is indicated by a slight horizontal ridge on the inside of the diencephalon. No infundibular process is yet indicated.

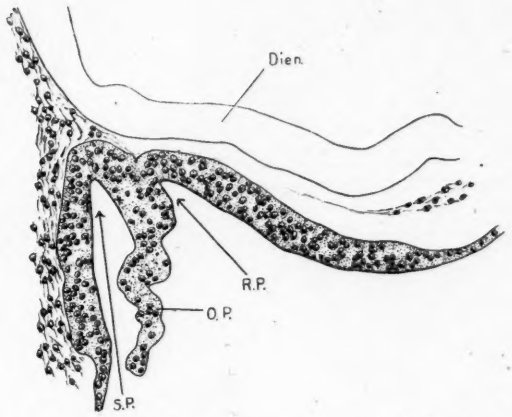

FIG. 14.—Stage I. *Trichosurus vulpecula* (1, *a*, 01). Median longitudinal section through the hypophysis and Seessel's pocket. Sl. 2-4-4.

Dien., diencephalic floor; O.P., oral plate; R.P., Rathke's pouch; S.P., Seessel's pocket.

STAGE II. *G.L.* 7 *mm.* (*Embryo a'* 97).—In this stage the limits of Rathke's pouch are clearly indicated by lateral grooves. The pouch is still widely open anteriorly, but its opening has narrowed considerably. Its roof is thick, its posterior closed portion is quadrilateral in transverse section, and its caudal extremity is slightly bifid.

The infundibular depression is relatively wide anteriorly, but becomes narrower posteriorly, indicating the form and position of the infundibular process.

A small rounded diverticulum situated caudal to the opening of Rathke's pouch represents the degenerating remnant of Seessel's pocket.

STAGE III. *G.L.* 7·5 *mm.* (*Embryo* XIX. 04).—The opening of Rathke's pouch has narrowed so as to form a short, wide duct, while the pouch itself is subdivided, in the portion behind the duct, by a pair of horizontal constrictions. The two lobes thus formed may be distinguished as proximal (*i.e.* nearest to the opening of the pouch, fig. 15, P.L.) and distal (*i.e.* nearest to the diencephalic floor, D.L.). The constriction disappears at the point where the hypophysial duct opens, so that the anterior, open section of the pouch is undivided. We shall see that the proximal lobe is destined to

form the pars tuberalis of the adult hypophysis, the remainder of the pouch forming the pars distalis and the pars infundibularis.

Both proximal and distal lobes in this stage are slightly bifid at their caudal extremity, the distal more markedly so than the proximal.

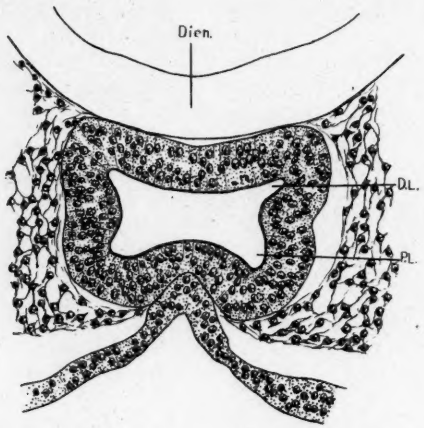

FIG. 15.—Stage III. *Trichosurus vulpecula* (XIX. 04). Transverse section through Rathke's pouch. Sl. 2-4-7.

D.L., distal lobe; Dien., diencephalic floor; P.L., proximal lobe.

STAGE IV. *G.L.* 7·25 *mm.* (XII. 02 *and* XII. A. 02).—The duct is here still further reduced, and anterior to it the pouch is relatively small and simple. The distal lobe is now considerably larger than the proximal, and extends further in the caudal direction (figs. 16 and 17). It is relatively extensive in the dorsi-ventral direction immediately caudal to the duct, and its walls are thick, consisting of a many-layered epithelium. Posterior to this it widens from side to side and becomes shallower, its dorsal wall becomes thin, while its lateral walls are thick and rather irregular. It is bifid posteriorly, the walls of the two halves being thin and forming a regular epithelium.

The proximal lobe (P.L.) is compressed dorso-ventrally, is wide from side to side, and is undivided posteriorly. The ventral wall is thin (fig. 16), its dorsal wall thicker.

A short conical infundibular process is present, fitting in between the two halves of the bifid caudal extremity of the distal lobe. Its walls, like those of the brain generally, consist simply of undifferentiated cells, uniformly distributed through its thickness. (*N.B.*—The infundibular process

is not shown in the longitudinal section figured, owing to the obliquity of the sectional plane.)

A small remnant of oral plate (fig. 17, O.P.) is present, arising from the postero-ventral wall of the proximal lobe. The narrowing of Rathke's pouch has occurred in such a way as to carry this remnant of oral plate within the opening of the pouch so that a remnant of Seessel's pocket (S.P.)

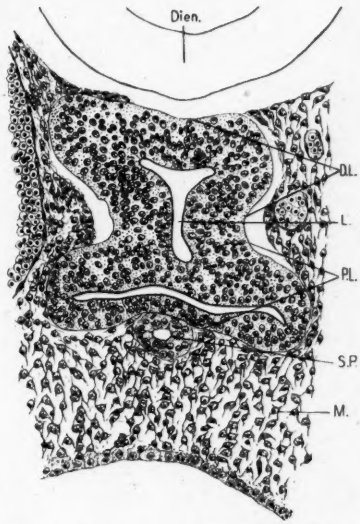

FIG. 16.—Stage IV. *Trichosurus vulpecula* (XII. 02). Transverse section through hypophysis. Sl. 5–2–8.

D.L., distal lobe; Dien., diencephalic floor; L., lumen; M., mesenchyme; P.L., proximal lobe; S.P., Seessel's pocket.

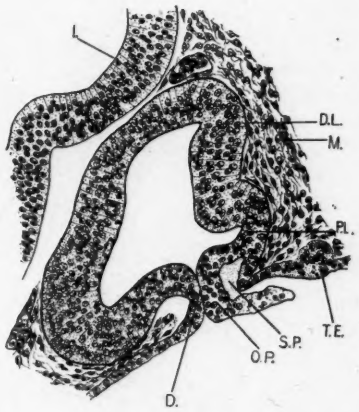

FIG. 17.—Stage IV. *Trichosurus vulpecula* (XII. A. 02). Longitudinal section through hypophysis. Sl. 8–3–2.

D., duct of Rathke's pouch; D.L., distal lobe; I., infundibular recess; M., mesenchyme; O.P., oral plate; T.E., transitory entodermal thickening; P.L., proximal lobe; S.P., Seessel's pocket.

is carried inwards and forms a small diverticulum on the posterior wall of the short duct. Thus it happens that portions of oral plate and of the entodermal wall of Seessel's pocket come to be included in the hypophysis at this stage.

STAGE V. *G.L.* 8·5 *mm.* (*Embryos* IV. 01 *and* 5′ 97).—The distal lobe (fig. 18, D.L.) has enlarged considerably, while the proximal lobe (P.L.) is much smaller relative to the whole buccal pouch. The duct is now reduced to a fine strand of cells. Seessel's pocket and the remnant of the oral plate have disappeared completely.

The proximal lobe, which lies entirely posterior to the remnant of the

duct, is wide from side to side, but very shallow dorsi-ventrally, with a small, cleft-like cavity. Its walls are thin and its lateral margins are slightly enlarged (L.P.L.). The lumen communicates with that of the main, distal lobe by a wide opening.

The distal lobe now constitutes the main bulk of the pouch, and its walls are distinctly thickened, except the portions which lie in actual contact with the infundibular process, these being thin (fig. 18, *c* and *d*). The

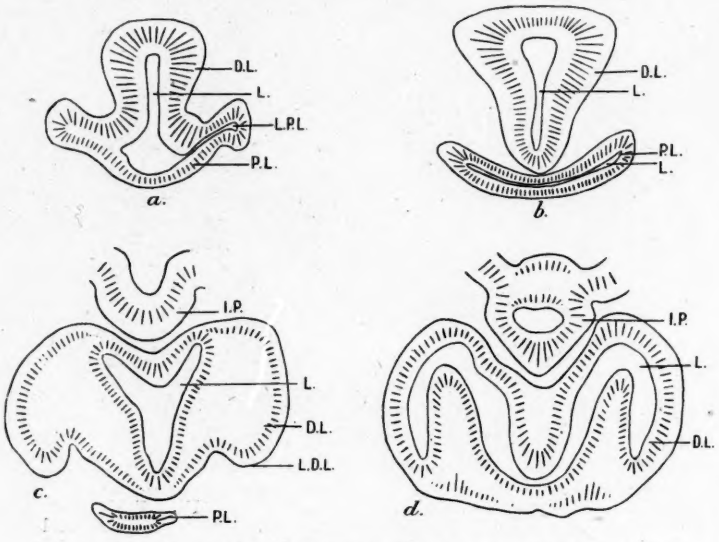

FIG. 18.—Stage V. *Trichosurus vulpecula* (IV. 01). Series of transverse sections through hypophysis, *a* being the most anterior, *d* the most posterior.

D.L., distal lobe; I.P., infundibular process; L., lumen; L.D.L., lateral expansion of distal lobe; L.P.L., lateral expansion of proximal lobe; P.L., proximal lobe.

lobe is rounded anteriorly, then becomes enlarged in the dorso-ventral direction (fig. 18, *a*). Posterior to the remnant of the duct, it has two large dorso-lateral hollow appendages (fig. 18 *c*, L.D.L.), whose cavities open into the main lumen. The distal lobe is still bifid caudally, and the infundibular process, which is a short, conical structure, fits in between the two halves. Its walls show no change since the preceding stage.

Up to this stage the most intimate relations between the diencephalic floor and the buccal pouch have been maintained, but in the longitudinal series of this stage there is a certain amount of mesenchymal tissue between the hypophysis and the brain floor in the region anterior to the

infundibular process. This latter is, however, in direct contact with the epithelial wall of the buccal pouch.

STAGE VI. *G.L.* 11 *mm.* (*Embryos* XXII. 01 *and* XXI. 04); *G.L.* 11·5 *mm.* (*Embryo* VII. 01).—The walls of the main distal lobe (D.L.)

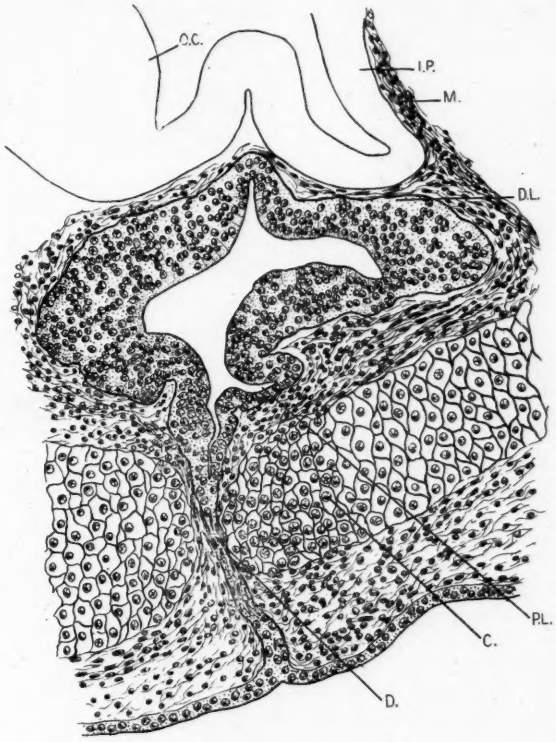

FIG. 19 —Stage VI. *Trichosurus vulpecula* (XXII. 01). Median longitudinal section through hypophysis. Sl. 11–2–1.

C., cartilage of skull; D., duct of Rathke's pouch; D.L., distal lobe; I.P., infundibular process; M., mesenchyme; O.C., optic chiasma; P.L., proximal lobe.

have now thickened considerably, so that in the region anterior to the duct only a small remnant of the lumen is present (figs. 19 and 20, L.).

The lumen enlarges in dorso-ventral extent in the middle portion of the hypophysis, and narrows again posteriorly. The dorso-lateral, wing-like expansions of the previous stage are still present, but their cavity is reduced to a small cleft, in open communication with the main lumen.

The walls consist of closely packed cells, showing no trace of differentiation or grouping.

The proximal lobe (fig. 20, P.L.) is crescentic in transverse section, with thin walls consisting of a regular epithelium. Its median portion contains a small, cleft-like cavity (L.), while its lateral wings (L.P.L.) are markedly enlarged and are produced backwards along the sides of the distal lobe.

In the posterior portion of the pouch, the dorsal wall is somewhat thin, and the bluntly conical infundibular process (fig. 19, I.P.), whose walls are still undifferentiated, fits into a depression in this wall. A thin layer of connective tissue has penetrated between the neural and buccal portions of the hypophysis in this stage.

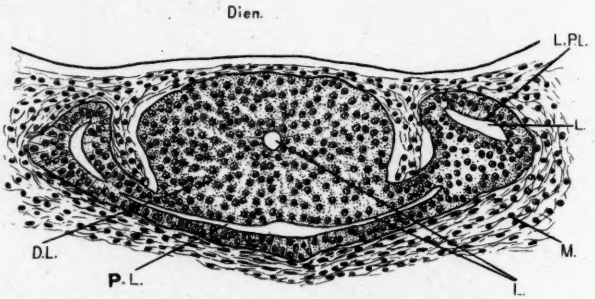

FIG. 20.—Stage VI. *Trichosurus vulpecula* (VII. 01). Transverse section through hypophysis. Sl. 4-1-9.

D.L., distal lobe; Dien., diencephalic floor; L., lumen; L.P.L., lateral expansion of proximal lobe; M., mesenchyme; P.L., proximal lobe.

No trace of Seessel's pocket is present.

STAGE VII. *G.L.* 13 *mm.* (*Embryos* IX. 01 *and* VIII. 01).—In general shape the hypophysis closely resembles that of the preceding stage, but it has increased considerably in size.

The walls of the anterior half of the distal lobe have increased in thickness, so that the lumen is reduced to a small, circular cavity (fig. 21, L.), while the extreme anterior end is solid. In the mid-portion of the hypophysis the lumen of the distal lobe increases in vertical extent, and still opens into the cavity of the proximal lobe. Posterior to this it expands into a triangular cavity (fig. 22, L.) with a thin roof (P.I.) and very thick sides; whilst in the hindermost portion the lateral walls also become thinner, the cavity spacious (fig. 23, L.), and the roof indented by the infundibular process (fig. 23, I.P.).

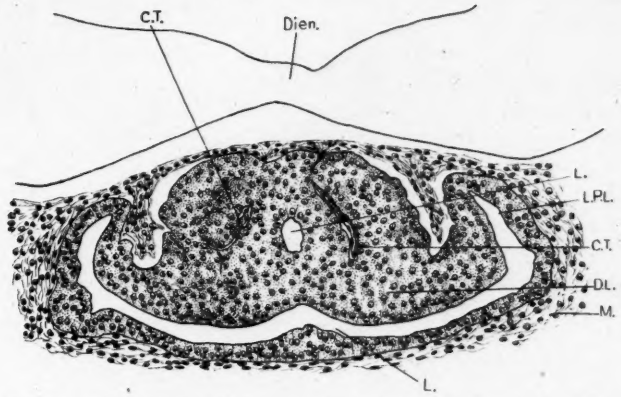

FIG. 21.—Stage VII. *Trichosurus vulpecula* (IX. 01). Transverse section through proximal and distal lobes of hypophysis. Sl. 4–5–10.

C.T., connective tissue; D.L., distal lobe; Dien., diencephalic floor; L., lumen; L.P.L., lateral expansion of proximal lobe; M., mesenchyme.

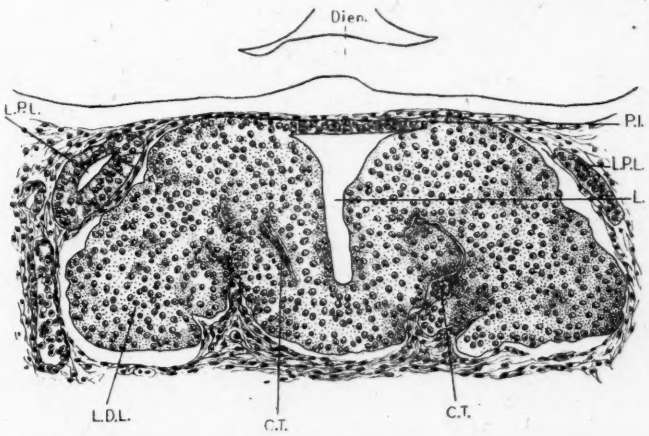

FIG. 22.—Stage VII. *Trichosurus vulpecula* (IX. 01). Transverse section through distal lobe in region of its lateral expansion. Sl. 5–1–6.

C.T., connective tissue; Dien., diencephalic floor; L., lumen; L.D.L., lateral expansion of distal lobe; L.P.L., lateral expansion of proximal lobe; P.I., portion of wall of pouch destined to form the pars infundibularis.

The proximal lobe is relatively and actually larger than in the preceding stage (fig. 21, P.L.). It is crescentic in transverse section, and has a

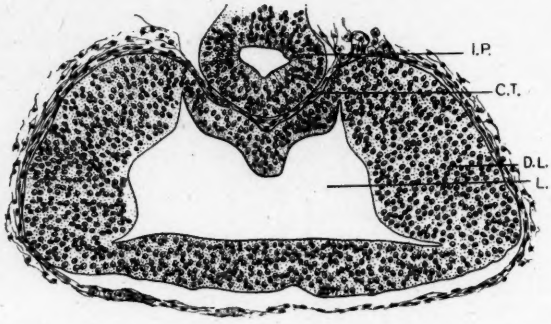

FIG. 23.—Stage VII. *Trichosurus vulpecula* (IX. 01). Transverse section through hypophysis in region of the infundibular process. Sl. 5-2-2.

C.T., connective tissue; D.L., distal lobe; I.P., infundibular process; L., lumen.

well-marked lumen. Its walls consist of a thin and regular epithelium, its dorsal wall has fused to a large extent with the distal lobe, while its lateral

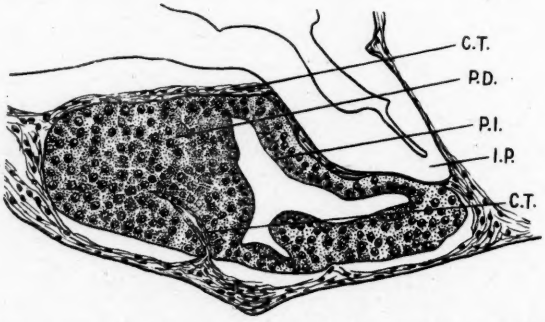

FIG. 24.—Stage VII. *Trichosurus vulpecula* (XXIV.). Median longitudinal section (reconstructed) through hypophysis. Sl. 7-1-2-4.

C.T., connective tissue; I.P., infundibular process; P.D., pars distalis; P.I., pars infundibularis.

margins (L.P.L.) have grown upwards towards the brain and are prolonged for some way posterior to its median portion (fig. 22, L.P.L.).

In this stage we can see the commencement of processes which convert the uniform walls of Rathke's pouch into the glandular "anterior lobe" of the typical adult hypophysis. In the more solid anterior portion of the

main lobe, thin strands of connective tissue (C.T.) are penetrating into the substance of the walls, sometimes carrying small blood-vessels with them. These strands grow in more or less symmetrically on either side of the middle line, so as to split the solid walls into lobules (figs. 21 and 22); and the cells also show a tendency to group themselves into cords or lobules, but with no indication of lumina. This lobulation only affects the anterior portion of the main lobe, the posterior portion thereof and the whole of the proximal lobe having thin uniform epithelial walls.

The infundibular process is fairly long, with a bluntly pointed apex (figs. 23 and 24, I.P.), and is separated from the buccal portion of the hypophysis by connective tissue (C.T.).

The duct is still present in one embryo of this stage, but is lost in the others, its site being marked by the perforation of the cartilage of the basis cranii.

In this stage the several portions of the adult hypophysis can now be identified. The pars neuralis (fig. 24, I.P.) is pressed against the dorsal wall of the pars buccalis, which itself consists of a juxta-neural portion (P.I.), represented by the thin wall in contact with the pars neuralis and the solid pars distalis (P.D.), already in process of conversion into a gland. The primordium of the pars tuberalis is represented by the lateral enlargements (fig. 21, L.P.L.) of the proximal lobe, the median portion of which subsequently becomes incorporated in the pars distalis. Thus the pars tuberalis is the only part which has not attained approximately its adult situation.

STAGE VIII. *G.L.* 15 *mm.*, *new-born* (*pouch fœtus* 5′ 97). — This stage shows a further advance in the process of breaking up of the solid walls of the hypophysis into lobules. In its main features the hypophysis closely resembles that of the preceding stage. The proximal lobe is much less distinct, its median portion being only represented by horizontal clefts (L., fig. 26) with a thin epithelial floor. Its lateral extensions (fig. 25, L.P.L.) are, however, considerably enlarged, and extend both anteriorly and posteriorly beyond their point of attachment, as hollow structures lying dorso-laterally to the main lobe (fig. 25, L.P.L.).

Ingrowths of connective tissue have broken up the walls of the anterior half of the distal lobe into rounded lobules (fig. 25), making the whole of the pars distalis appear less compact and less uniform than in preceding stages.

The infundibular process is rounded or slightly triangular in transverse section. It narrows to a definite stalk, connecting it with the diencephalic floor. There is a small amount of connective tissue between the infundibular process and the pars buccalis.

A remnant of the duct persists, and a thinning of the cartilage below the hypophysis marks the site of its perforation by the duct.

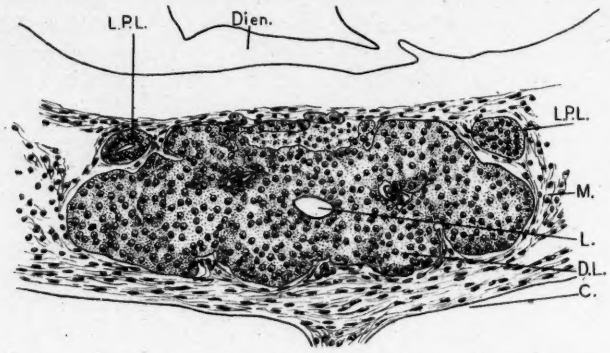

FIG. 25.—Stage VIII. *Trichosurus vulpecula* (5′ 97). Transverse section through anterior portion of distal lobe. Sl. 3–5–2.

C., cartilage; D.L., distal lobe; Dien., diencephalic floor; L., lumen; L.P.L., later expansions of proximal lobe; M., mesenchyme.

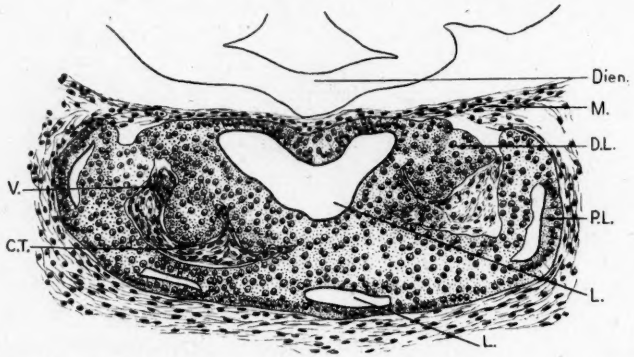

FIG. 26.—Stage VIII. *Trichosurus vulpecula* (5′ 97). Transverse section through proximal and distal lobes. Sl. 3–5–7.

C.T., connective tissue; D.L., distal lobe; Dien., diencephalic floor; L., lumen; M., mesenchyme; P.L., proximal lobe; V., blood-vessel.

STAGE IX. *Pouch fœtus G.L.* 17 *mm., and pouch fœtus G.L.* 17·5 *mm.*— The pars buccalis is now converted into a relatively compact structure, *i.e.* there is little indication externally of subdivision into lobes. The proximal lobe is, however, still represented in the middle line by a small, horizontal cleft, while the lateral wings are still further enlarged.

There is a considerable main lumen, which is restricted to the posterior half of the pars buccalis. The walls of the pars distalis consist of masses of cells more or less completely split up into lobules, separated by connective tissue carrying blood-vessels. The pars juxta-neuralis (infundibularis) consists of a thin epithelial layer, lying close to the infundibular process, but separated therefrom by connective tissue.

The infundibular process closely resembles that of the preceding stage, and still contains a well-marked lumen.

Remnants of the duct are present, and the point of perforation of the cartilage is still clear in one embryo.

STAGE X. *Pouch fœtus, H.L.* 11 *mm., and pouch fœtus H.L.* 12·5 *mm.*— The hypophysis has now attained its adult condition in regard to the general arrangement of the parts. Its subsequent development consists chiefly in histological differentiation in the various regions.

The pars buccalis (fig. 27) is clearly differentiated into pars distalis and pars juxta-neuralis, including infundibular (P.I.) and tuberal (P.T.) portions. The latter has now assumed its definitive position lying between the pars distalis and the diencephalic floor (T.C.), but is as yet restricted to the region anterior and lateral to the hypophysial stalk (figs. 27 and 28, P.T.).

The bulk of the organ is constituted by a compact pars distalis derived from the ventral, antero-, and postero-ventral walls of the pars buccalis of earlier stages. This is continuous on its dorsal side with the thin layer of epithelium constituting the infundibular portion of the pars juxta-neuralis (P.I.) and forming the roof of the residual lumen (L.) which forms a cup-shaped cleft surrounding the infundibular process. (Compare figs. 27 and 28, L.) There is a relatively small portion of the pars tuberalis (P.T.) in the median line, but on either side of the hypophysial stalk it has attained considerable dimensions (fig. 28, P.T.).

The pars distalis consists of a compact mass of solid cords of cells, many of which are outlined and separated from each other by strands of connective tissue which can be traced inwards from the sheath surrounding the pars buccalis. The nuclei of the cells of the pars distalis are spherical and deeply stained. The cytoplasm of the majority of the cells is stained faintly blue, but there are also a number of cells whose cytoplasm is stained a distinct reddish colour. These red cells appear to correspond with the chromophilic cells described in the hypophysis by histologists. They appear in this stage for the first time in Trichosurus, and, as will be seen from fig. 27, are most numerous in the posterior portion of the pars distalis. They appear in greater numbers and show their peculiar staining capacity in a more marked degree in the later stages of Dasyurus and Phascolarctos.

The infundibular portion of the pars juxta-neuralis (P.I.) consists of a

thin layer of epithelium closely investing the pars neuralis on its anterior, ventral, and lateral surfaces, but leaving its postero-dorsal face exposed. In transverse sections this layer forms about three-fourths of a circle, surrounding the infundibular process, and also forms both walls of the dorso-lateral horns of the crescentic residual lumen (fig. 28). It is slightly thickened in the region where it joins the lateral masses of the pars distalis.

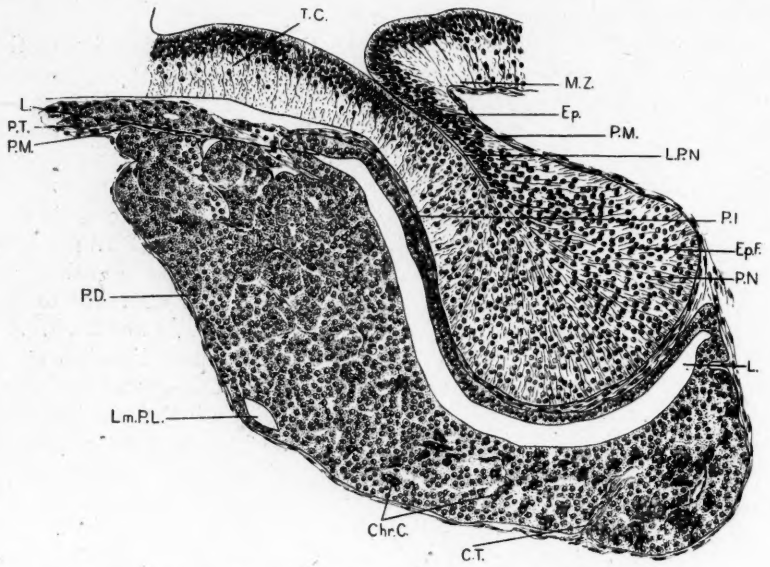

FIG. 27.—Stage X. *Trichosurus vulpecula* (H.L. 12·5 mm.). Median longitudinal section through hypophysis. Sl. 11-1-5.

C.T., connective tissue; Chr.C., chromophilic cells; Ep., ependyma; Ep.F., ependymal fibres; L., lumen; L.P.N., lumen of pars neuralis; Lm.P.L., remnant of lumen of proximal lobe; M.Z., marginal zone; P.D., pars distalis; P.I., pars infundibularis; P.M., pia mater; P.N., pars neuralis; P.T., pars tuberalis; T.C., tuber cinereum.

At its anterior extremity, the pars infundibularis is prolonged into a pocket-like diverticulum, projecting towards the pars tuberalis and lying between the tuber cinereum and the pars distalis (fig. 27, L.). The epithelium of the pars juxta-neuralis consists of two or three layers of cells with very darkly staining nuclei.

The pars tuberalis is the direct derivative of the enlarged lateral portions of the proximal lobe of earlier stages. The proximal lobe is no longer complete, but portions of it remain. A small cleft on the ventral side of the pars distalis (fig. 27, Lm.P.L.) represents the remnant of its median

cavity, whilst the tubules of the pars tuberalis are connected on one side at least with the pars distalis by a solid cord of cells which runs round the side of the pars distalis and joins it ventro-laterally. This is clearly the remnant of the hollow, crescent-shaped portion of the proximal lobe. Its dorso-lateral wings have enlarged markedly, grown up towards the brain and branched, so that they now form a series of thin-walled tubules which have penetrated between the pars distalis and the tuber cinereum. Anterior to the pocket-like diverticulum of the pars infundibularis, they actually reach the middle line; in the region of the diverticulum, they lie on either

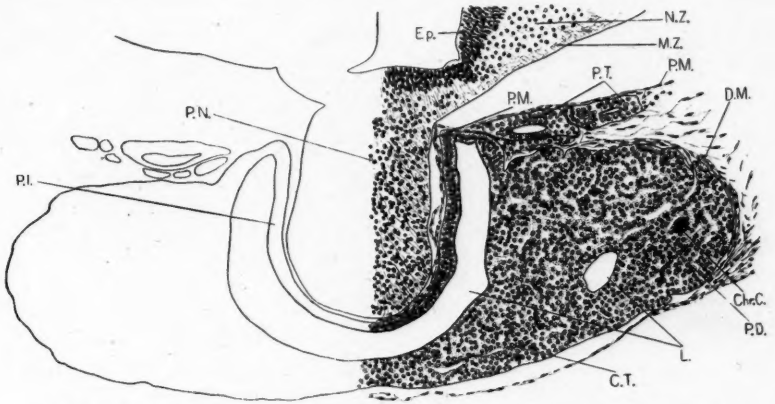

FIG. 28.—Stage X. *Trichosurus vulpecula* (H.L. 11 mm.). Transverse section through hypophysis. Sl. 10-1-2.

C.T., connective tissue; Chr.C., chromophilic cells; D.M., dura mater; Ep., ependyma; L., lumen; M.Z., marginal zone; N.Z., nuclear zone; P.D., pars distalis; P.I., pars infundibularis; P.M., pia mater; P.N., pars neuralis; P.T., pars tuberalis.

side of it; posterior to it, they lie lateral to the stalk of the pars neuralis (see fig. 28, P.T., etc.). The walls of the tubules consist of two or three layers of epithelial cells whose nuclei are deeply stained, while their cytoplasm in its staining capacity resembles the lightly stained cells of the pars distalis.

The infundibular process is connected with the floor of the diencephalon by a relatively stout stalk. It is enlarged distally (fig. 27, P.N.), and contains a small lumen in the 12·5 mm. (H.L.) embryo (fig. 27, L.P.N.), but is solid in the 11 mm. (H.L.) embryo. The ependymal layer of the diencephalic floor is continuous with that of the infundibular stalk, and extends a short way into the substance of the pars neuralis, the bulk of which is made up of fibres and scattered cells closely resembling those of the nuclear (mantle) zone of the diencephalic wall (fig. 28, N.Z.).

The connective tissue separating the nervous and non-nervous portions of the hypophysis exhibits a tendency to penetrate into the tissues of the pars neuralis, but has not as yet done so to any marked extent, nor is there any sign of blood-vessels entering the nervous lobe at this stage.

STAGE XI. *Pouch fœtus G.L.* 4 *cm., H.L.* 20 *mm.*—The hypophysis in this fœtus closely resembles that of the preceding stage in form and general relations of the parts. It has increased considerably in size, both pars buccalis and pars neuralis being much larger than in the

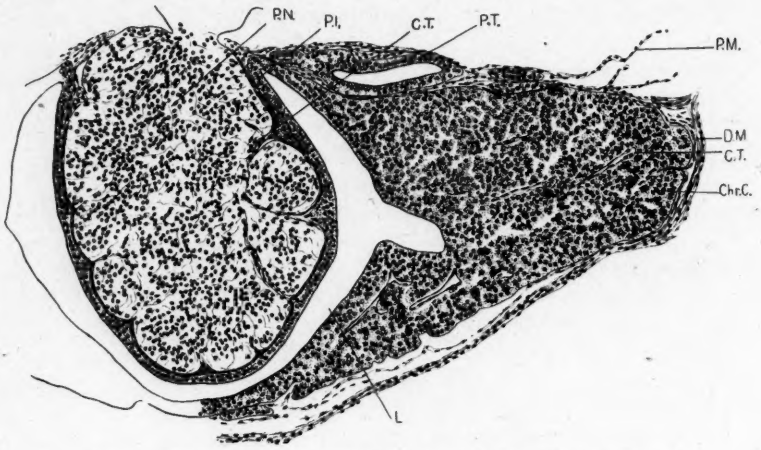

FIG. 29.—Stage XI. *Trichosurus vulpecula* (H.L. 20 mm.). Transverse section through hypophysis. Sl. 23-3-5.

C.T., connective tissue; Chr.C., chromophilic cells; D.M., dura mater; L., lumen; P.I., pars infundibularis; P.M., pia mater; P.N., pars neuralis; P.T., pars tuberalis.

preceding stage, whilst the process of histological differentiation has made considerable progress.

The number of chromophilic cells (fig. 29, Chr.C.) in the pars distalis has increased considerably, especially in the posterior portion of that part. Moreover, these cells are now more clearly differentiated from the chromophobic cells, their cytoplasm staining a bright red, while that of the chromophobic cells is stained faint blue.

The pars tuberalis (P.T.) has increased to such an extent that it has spread into the narrow space between the pars buccalis and the diencephalic floor so as to completely encircle the hypophysial stalk (*cf.* fig. 13). Thus it comes to have the form described by Tilney (59), viz. that of a diaphragm lying between the pars distalis and the diencephalon, with the stalk of the pars neuralis passing through its aperture.

It is in the pars neuralis (fig. 29, P.N.) and the pars infundibularis (P.I.) that we find the most marked advance on the preceding stage. The distal portion of the pars neuralis has expanded considerably, while its attachment to the diencephalic floor is relatively slender. The connective tissue between these two portions has grown actively and penetrated into the tissues of the pars neuralis, breaking it up more or less completely into lobules (fig. 29, P.N.). Furthermore, it tends to carry in with it some of the cells of the pars infundibularis, so that whilst the outer side of that layer, *i.e.* that bordering the residual lumen, is still perfectly regular, the inner margin is irregular, the cells here and there penetrating a short way into the tissues of the pars neuralis. Over the greater part of its extent, however, the pars infundibularis simply consists of a single layer of epithelium.

The pars neuralis still contains a large number of cells, but its fibrous constituents have become much more conspicuous.

Capillaries do not appear as yet to have penetrated into the pars neuralis; indeed, the pars buccalis is not yet richly vascularised.

The relations of the meninges are as follows (figs. 13 and 29, D.M., P.M.):—The dura mater (D.M.) forms a connective tissue capsule for the whole of the pituitary body. The main portion passes straight round on the ventral surface of the whole structure, thus enclosing it within the same membrane with the brain. At the anterior and posterior ends of the pituitary a considerable thickness of the dura mater is reflected over the dorsal surface of the pars buccalis, but this layer extends in towards the hypophysial stalk through only a few sections. In the remainder of the pars distalis a few fibres pass round on to the dorsal surface of the lobe, and even penetrate inwards to the middle line, except in the region of the hypophysial stalk. The pia mater (P.M.) constitutes a very thin layer covering the brain and passing continuously over the surface of the pars neuralis, lying between it and the pars juxta-neuralis and penetrating into the substance of the nervous lobe in the manner already described. The pia mater also completely invests the tubules of the pars tuberalis and penetrates between them.

Phascolarctos cinereus.—In many respects the development of the hypophysis of Phascolarctos closely resembles that of Trichosurus. It shows, however, one or two points of interest, notably the persistence of Seessel's pocket. I have accordingly described such stages in development as serve to illustrate these points.

Stage I. *G.L.* 4 *mm.*—The hypophysis is already developed as a wide pouch, fairly deep posteriorly where it is closed, but shallow and widely open in its anterior portion. It is very noticeably bilobed (*cf.* fig. 30),

the lateral angles being thick-walled, while in the middle line the epithelium is much thinner.

There is a small remnant of the oral plate, posterior to which lies Seessel's pocket, in the form of a short, rounded diverticulum of the fore-gut, whose tip lies between the floor of the hypophysis and the wall of the gut.

No infundibular process is present, and from the fact that the diencephalon is still unclosed it is evident that the hypophysis appears at an earlier stage in Phascolarctos than it does in Trichosurus.

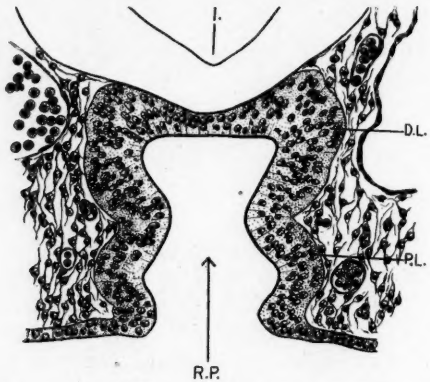

FIG. 30.—Stage II. *Phascolarctos cinereus.* Transverse section through Rathke's pouch. Sl. 5–11–2. Note the markedly thickened lateral angles of Rathke's pouch.

D.L., distal lobe ; I., infundibular recess ; P.L., proximal lobe ; R.P., Rathke's pouch.

STAGE II. *G.L.* 7·5 *mm.*—In this stage we find a remarkable development of the pre-oral gut.

The hypophysis forms a deep pouch, which is differentiated anteriorly into proximal and distal lobes by a well-marked equatorial constriction.

The oral plate is ruptured ventrally, but a considerable portion of it persists dorsally, being inserted at the apex of Rathke's pouch and separating this from the pre-oral gut. The oral plate is slightly convex on its posterior face, so that in the sections immediately behind that which passes through its full expanse, the convex projection of the oral plate is cut and appears in section as a sort of plug (cf. *Perameles nasuta*, (13 VII. 05), fig. 5). The section represented in fig. 31 passes through almost the complete expanse of oral plate dorsally, and shows the ventral portion of the oral plate projecting into Seessel's pocket.

Seessel's pocket forms a vesicle of considerable dimensions (figs. 31 and 32, S.P.) opening by a small duct immediately posterior to the oral plate. It is of the same depth as the hypophysis, and its distal wall is in actual contact with the diencephalic floor (fig. 32, Dien.), whilst it also, like Rathke's pouch, shows an indication of an equatorial constriction.

Its walls are thick, and are composed of a regular, columnar epithelium.

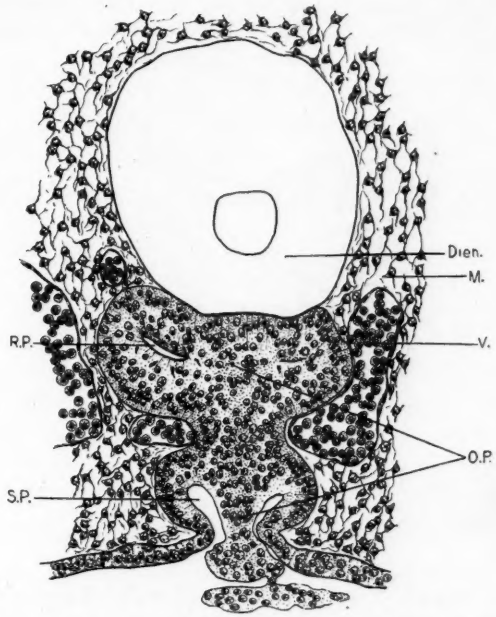

FIG. 31.—Stage II. *Phascolarctos cinereus*. Transverse section through hypophysis, Seessel's pocket, and the oral plate. Sl. 5-1-5.

Dien., diencephalic floor; M., mesenchyme; O.P., oral plate; R.P., Rathke's pouch; S.P., Seessel's pocket; V., blood-vessel.

Histologically it is, in fact, indistinguishable from the hypophysis. The anterior extremity is pressed against the posterior wall of Rathke's pouch, which is thereby indented slightly in the middle line.

A rounded depression in the diencephalic floor represents the primitive infundibular recess, but no infundibular process is yet differentiated.

The notochord in this embryo reaches actually to the level of the posterior wall of Seessel's pocket, but is not in actual contact therewith.

STAGE III. *G.L.* 9 *mm.*—The hypophysis has increased considerably

in size, but is still widely open anteriorly and consists of proximal and distal lobes.

A definite infundibular process is present in the form of a short conical outgrowth of the diencephalic floor (fig. 34, I.P.). This is in intimate contact with both Rathke's pouch and the pre-oral gut (*vide infra*).

Remnants of the oral plate are present in the form of a solid, knob-like mass of tissue lying outside the pouch and a small portion lying free in the lumen of Rathke's pouch.

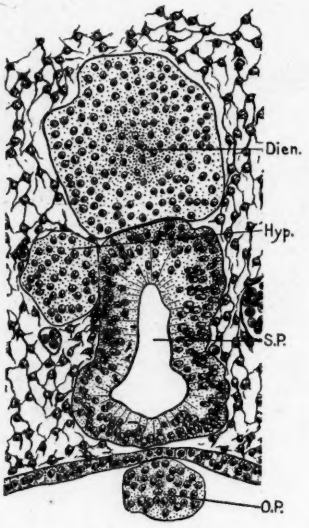

FIG. 32.—Stage II. *Phascolarctos cinereus.* Transverse section through Seessel's pocket. Sl. 5–1–2.

Dien., diencephalic floor; Hyp., posterior wall of one of lateral caudal lobes of the hypophysis; O.P., oral plate; S.P., Seessel's pocket.

Seessel's pouch has lost its opening into the gut and simply forms a closed, hollow vesicle, in intimate contact with Rathke's pouch, but having no communication with it. It is elongated in the antero-posterior direction, and is divided as before into two lobes, whose cavities are now completely separate from each other. Its walls consist, as before, of regular columnar epithelial cells, and resemble those of the hypophysis so closely that in the posterior region, where Rathke's pouch is bifid and Seessel's pocket lies between the two halves, there appear to be three precisely similar lobes of the hypophysis (fig. 34).

Anterior to the point of bifurcation of Rathke's pouch, the pre-oral gut is excluded from contact with the brain floor. It is constricted in this region and has no lumen, but widens again anteriorly and has a small, cleft-like cavity (fig. 33, S.P.). At one point (fig. 33) it is partially separated from Rathke's pouch by a small blood-vessel, but elsewhere the walls of the two structures are in close contact.

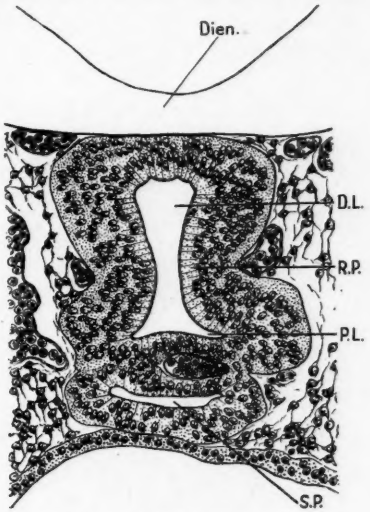

FIG. 33.—Stage III. *Phascolarctos cinereus*. Transverse section through Rathke's pouch and Seessel's pocket. Sl. 4-4-3.

D.L., distal lobe; Dien., diencephalic floor; P.L., proximal lobe; R.P., Rathke's pouch; S.P., Seessel's pocket.

STAGE IV. *G.L.* 11 *mm.*—This stage shows the beginning of the process of formation of tubules. Unfortunately, the series is broken in the region of the hypophysis, so that it is impossible to give a full description.

The walls of the distal lobe in Phascolarctos, instead of undergoing subdivision by ingrowths of connective tissue, as occurs in Trichosurus, proliferate actively and give off numerous outgrowths which penetrate into the connective tissue surrounding the hypophysis (fig. 35). The proximal lobe is much curved (fig. 35, P.L.), so that its lateral margins, which are enlarged and prolonged both anteriorly and posteriorly, lie dorso-lateral to the main lobe (L.P.L.).

Seessel's pocket is still present, and forms a closed vesicle with a small,

cleft-like lumen. It is much flattened, and is applied to the ventral surface of the hypophysis (S.P.).

STAGE V. *G.L.* 12·25 *mm.*—In this stage the process of conversion of the simple buccal pouch into the compact glandular lobe of the adult is proceeding.

The posterior portion of the pars buccalis has fairly uniform thick walls and a large lumen. Its dorsal wall is indented by the infundibular process. The walls of the anterior portion of the main lobe are produced into numerous outgrowths, some of which now possess a small lumen.

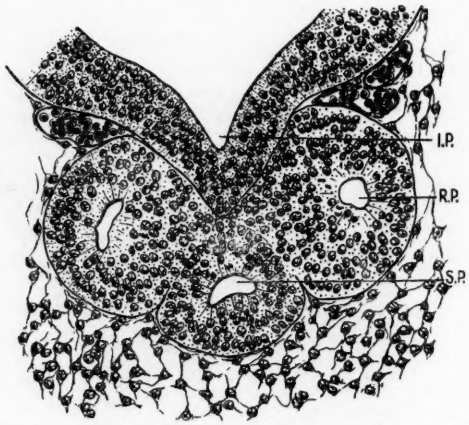

FIG. 34.—Stage III. *Phascolarctos cinereus* (9 mm.). Transverse section through posterior portion of Rathke's pouch and Seessel's pocket. Sl. 4–2–7.

I.P., infundibular process; R.P., Rathke's pouch; S.P., Seessel's pocket.

The spaces between these processes are filled with connective tissue in which as yet there are few blood-vessels. The proximal lobe shows the same relations as in the preceding stage. Its walls are produced into a few short solid processes.

The infundibular process is short and conical, and a certain amount of connective tissue has penetrated between it and the pars buccalis, but has not yet reached the middle line.

Seessel's pocket forms a closed vesicle in the same position as in the preceding stage. At its posterior end it increases in dorso-ventral extent, forming a rounded vesicle with thick walls and a small lumen. Anteriorly it becomes flattened and widens out so as to form a thin plate with a cleft-like lumen, while its dorsal wall is confluent with the substance of the

rest of the pars distalis. Its lumen, however, does not communicate with that of the hypophysis.

The pre-oral gut therefore now forms an apparent part of the hypophysis, from which it can only be distinguished by a slight difference in staining capacity and by the fact that its lumen, unlike any portion of the main lumen of the pars buccalis, is completely isolated.

A small remnant of the hypophysial duct is present in this stage, lying

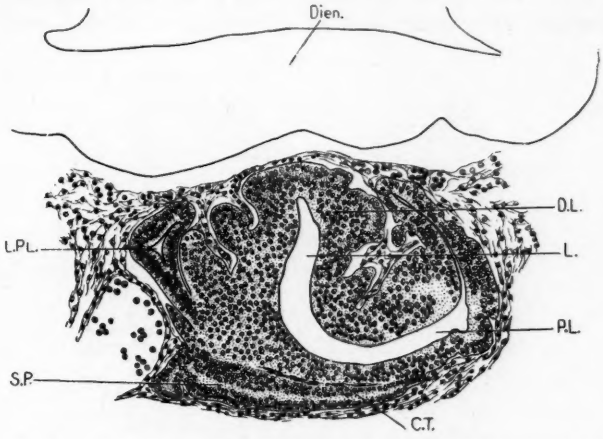

FIG. 35.—Stage IV. *Phascolarctos cinereus* (11 mm.). Transverse section through proximal and distal lobes of hypophysis. Sl. 6-1-10.

C.T., connective tissue; D.L., distal lobe; Dien., diencephalic floor; L., lumen; L.P.L., lateral enlargement of proximal lobe; P.L., proximal lobe; S.P., Seessel's pocket.

outside the cartilage of the skull, but there is no trace of it within the skull, nor any indication of perforation of the cartilage.

STAGE VI. *GL.* 13·5 *mm.: longitudinal and transverse series.*—In general form the hypophysis in this stage closely resembles that of the preceding, but the process of tubule-formation has increased so far as to convert the distal portion of the pars buccalis into a compact mass of tubules separated from each other by connective tissue (fig. 36).

The minute structure of the pars buccalis differs considerably in this stage from that of any stage of Trichosurus. Fig. 36, which represents a longitudinal section about 6–8 sections (15μ) from the middle line, shows this structure. In place of the solid, irregular, and ill-defined lobules of Trichosurus, the cells are arranged in a series of relatively definite tubules (T.), some of which possess a lumen (L.i.), while the outline of these tubules, instead of being indicated simply by a cleft, is marked by a definite though

fine line, representing a basement membrane of the cells constituting the walls of the tubules.

The infundibular process is narrow and pointed, and is separated from the pars buccalis by connective tissue, which has penetrated to the middle line in some places.

Seessel's pocket can be readily identified, and has undergone no change since the preceding stage.

STAGE VII. *G.L.* 16·5 *mm.: new-born.*—This stage shows little advance on the preceding. The pars distalis has become more compact,

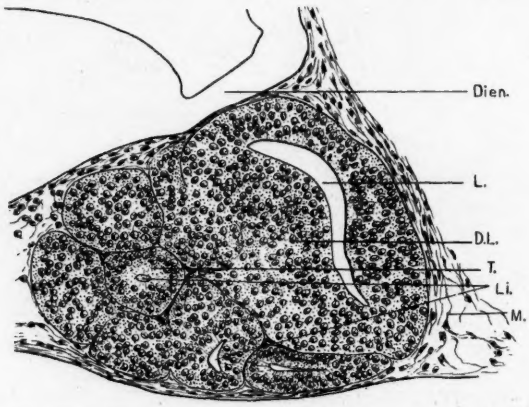

FIG. 36.—Stage VI. *Phascolarctus cinereus* (13·5 mm.). Longitudinal section through hypophysis. Sl. 12–2–7.

D.L., distal lobe; Dien., diencephalic floor; L., lumen of pars distalis; L.i., lumina of tubules; M., mesenchyne; T., tubule of pars distalis.

its tubules having increased in size and number and become pressed more closely together.

The lateral portions of the proximal lobe have grown round the main body of the pars buccalis, and now lie almost entirely dorsal thereto.

Seessel's pocket is clearly recognisable. As before, it is dorso-ventrally compressed and wide anteriorly, while posteriorly it forms a vesicle triangular in section and having a small lumen.

STAGE VIII. *Pouch fœtus G.L.* 17 *mm.*—A noticeable feature of this stage is the very rich supply of capillaries to the pars distalis. They occupy the spaces between the tubules, and have also penetrated between the infundibular process and the pars buccalis. A pair of small vessels, symmetrically disposed, enter the pars distalis on its ventral surface. The distal lobe in this, as in other similar stages of Phascolarctos and in Trichos-

urus (*cf.* fig. 22), is produced into two large wing-like processes, and the blood-vessels enter on the under side of these and penetrate deeply into the tissue of the lobe. Another vessel enters in the middle of the posterior wall of the pars buccalis.

The lateral prolongations of the proximal lobe are now branched (fig. 37), and form a collection of tubules lying dorsal and dorso-lateral to the rest of the pars buccalis. These constitute the primordium of the pars tuberalis (P.T.).

It is not possible in this embryo to identify Seessel's pocket with certainty.

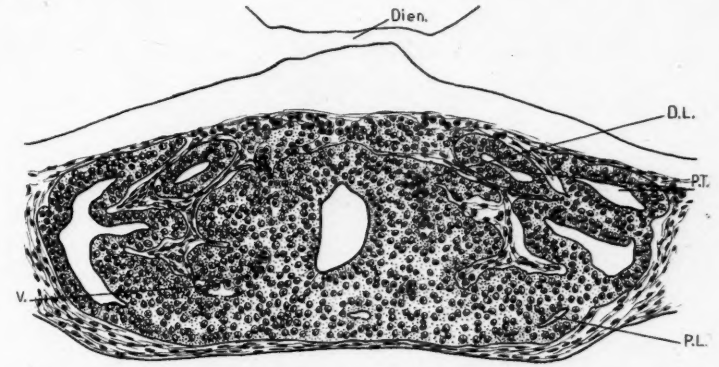

FIG. 37.—Stage VIII. *Phascolarctos cinereus* (17 mm. G.L.). Transverse section through proximal and distal lobes of hypophysis, to show the branched lateral expansions of the former (primordium of pars tuberalis). Sl. 3-2-8.

D.L., distal lobe; Dien., diencephalic floor; P.L., proximal lobe; P.T., primordium of pars tuberalis; V., blood-vessel.

STAGE IX. *Pouch fœtus G.L.* 18 *mm.*—The series is broken in the region of the hypophysis, but it is worth noting that Seessel's pocket is clearly recognisable and has exactly the same form and relations as in Stage VII.

STAGE X. *Pouch fœtus G.L.* 18·5 *mm., H.L.* 9·5 *mm.*—This stage shows in general little advance on the preceding. The pars buccalis is somewhat more compact, its tubules being closely pressed together. In this stage for the first time chromophilic cells can be identified in the pars distalis. They are very brightly stained, and are most numerous in the posterior region.

The lateral wings of the proximal lobe are slightly less branched than in the preceding stage.

The infundibular process is small relatively to the size and advanced

condition of the pars buccalis. It forms a simple, thin-walled diverticulum with a somewhat constricted neck.

It is not possible to identify Seessel's pocket with absolute certainty in this stage. A small, flattened structure, closely resembling Seessel's pocket in other embryos, is present, but is in such close relation to the proximal lobe that it is impossible to draw an absolute distinction between the two structures.

STAGE XI. *Pouch fœtus G.L.* 24 *mm., H.L.* 11·5 *mm.*—The hypophysis has increased markedly in size. The tissue of the pars distalis has un-

FIG. 38.—Stage X. *Phascolarctos cinereus* (H.L. 11·5 mm.). Transverse section through pars distalis. Sl. 10–1–3.

C.T., connective tissue; Chr.C., chromophilic cells; L., lumen; P.I., pars infundibularis; S.P., Seessel's pocket.

fortunately shrunk away somewhat from the connective tissue, which now forms an interlacing network penetrating throughout the substance of the pars distalis. The appearance of compactness is accordingly destroyed.

The pars distalis consists of numerous rounded lobules, all of which have now lost their lumina. The cells are very clearly differentiated into chromophilic (Chr.C.) and chromophobic types, the former showing up as clear bright-red patches in the tissue (represented black in figures).

The pars tuberalis forms a collection of branched tubules lying between the body of the pars distalis and the diencephalic floor anterior to the infundibular process. It is still connected by a cell cord with the ventral side of the pars buccalis.

The infundibular process has increased somewhat in size, but is still relatively small, and is hollow. Its walls have increased in thickness to a slight extent.

Seessel's pocket can be clearly identified in the posterior portion of the hypophysis. Its caudal portion is free, and is separated from the substance of the pars buccalis by a definite connective tissue sheath. Its caudal extremity retains its original form and relations, lying partly

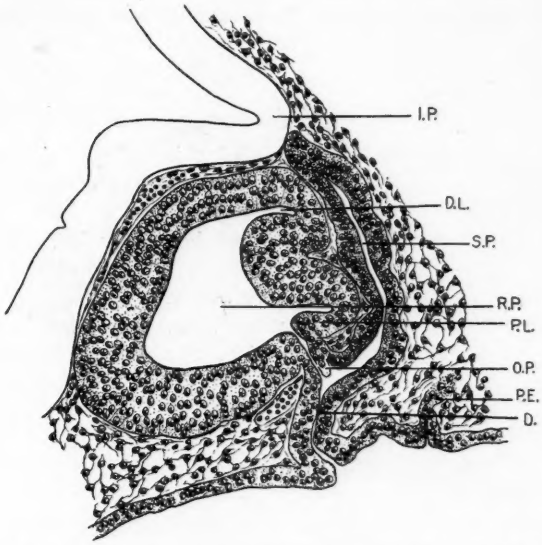

FIG. 39.—Stage I. *Phascolomys mitchelli* (G.L. 8·5 mm.). Longitudinal section through hypophysis and Seessel's pocket. Sl. 8–2–8.

D., duct; D.L., distal lobe; I.P., infundibular process; O.P., remnant of oral plate; P.E., proliferation of entoderm; P.L., proximal lobe; R.P., Rathke's pouch; S.P., Seessel's pocket.

ventral to and between the two halves of the posterior extremity of the pars buccalis. The anterior portion of Seessel's pocket fuses with the ventral side of the pars distalis and becomes absolutely indistinguishable from it (fig. 38, S.P.).

Phascolomys mitchelli.—In Phascolomys also Seessel's pocket persists and forms part of the hypophysis, but certain points of difference may be noted between the development in this form and in Phascolarctos.

STAGE I. (*a*) *G.L. 9 mm.*—Rathke's pouch is already established, and closely resembles that of Phascolarctos, Stage II., having well-marked

proximal and distal lobes. It is widely open in its mid-region, but is closed at both anterior and posterior ends.

No definite infundibular process is present.

The distal lobe of Rathke's pouch is bifid at its caudal extremity, and lying between the two halves is a well-developed Seessel's pocket, which in this instance differs considerably from Rathke's pouch in its staining capacity. It is a hollow, conical structure, its walls being composed of a regular epithelium, the cells staining more darkly than those of the hypophysis. It runs forwards, ventral to the hypophysis and in the middle line, for a short distance, and then twists to one side. In correlation with this asymmetry, the remnant of oral plate is displaced from its normal plane and lies obliquely, forming, as usual, the partition wall between Seessel's pocket and the hypophysis.

(*b*) *G.L.* 8·5 *mm.*—The hypophysis of this embryo differs from that described above mainly in the fact that the opening of Rathke's pouch is reduced to a narrow duct (fig. 39, D.).

Seessel's pocket (S.P.) has retained its original relations, but the elongation of the duct has taken place ventral to the opening of the pre-oral gut, *i.e.* between the base of that structure and the pharyngeal roof, so that there is a relatively long and narrow duct (D.) which is common to both Seessel's pocket and the hypophysis. A small remnant of oral plate (O.P.) can still be recognised attached to the posterior wall of Rathke's pouch, at its point of junction with Seessel's pocket.

It may be noted that in both the 8·5 mm. and the 9 mm. embryos there is a small entodermal outgrowth (fig. 39, P.E.) posterior to Seessel's pocket.

This structure is a thin tubular diverticulum, and closely resembles the hypophysial duct. It has a minute lumen opening into the pharynx, is very short, and tapers to a blind extremity. I have not observed the occurrence of this structure in other species, unless it corresponds with the entodermal proliferation shown in fig. 17 of Trichosurus, Stage IV.

In a later stage of Phascolomys (15·5 mm. G.L.) there is possibly a trace of it still indicated by the fact that the cartilage is perforated at two points. Through the anterior of these perforations the hypophysial duct passes, whilst on the pharyngeal side of the second there is a small diverticulum, possibly representing a remnant of the structure described above.

In its subsequent stages the hypophysis of Phascolomys very closely resembles that of Phascolarctos. The walls of the pouch grow out as solid processes which become pressed together to form the compact pars distalis. The origin of the pars tuberalis is exactly the same as in Phascolarctos.

Seessel's pocket is still recognisable in an embryo of 17·5 mm. G.L., but no later stages are available.

In Phascolomys the extremely rich vascular supply to the pars distalis in stages of 15·5 mm. G.L. and 17·5 mm. G.L. is noteworthy, and is even more marked than in Phascolarctos at similar stages.

Dasyurus viverrinus.—A series of Dasyurus stages, from the establishment of Rathke's pouch to a stage in which the infundibular process has become solid, is available, and from study thereof it is evident that the development of the hypophysis in Dasyurus closely resembles that process in Trichosurus. With regard to the process of conversion of the simple pouch into the glandular lobe of the adult, Dasyurus seems to be in some respects intermediate between Trichosurus and Phascolarctos, for both outgrowth of solid processes and ingrowth of connective tissue play a part in the elaboration of the gland. After the establishment of Rathke's pouch and its subdivision into proximal and distal lobes, its walls become considerably thickened and produced into short rounded processes. At the same time the walls are subdivided by ingrowths of connective tissue so that the two processes occur contemporaneously.

A definite infundibular process appears relatively early in Dasyurus, viz. in a stage corresponding approximately to Trichosurus, Stage IV., where it forms a relatively long, conical diverticulum.

There is no trace of Seessel's pocket in Dasyurus subsequent to the last stage described in Section I. of this paper.

From the more complete series of late stages in Dasyurus it is possible to make out some points, more particularly with regard to the infundibular process, which are not shown in the Trichosurus series. I propose, therefore, to give a brief description of the three oldest stages of *Dasyurus viverrinus.*

Stage H. *Pouch fœtus, G.L.* 13·5 *mm., H.L.* 8 *mm.*—In the general arrangement of the parts, this stage closely resembles Trichosurus, Stage X.

From the longitudinal section (fig. 40) it will be seen that the pars buccalis extends further round on to the posterior side of the infundibular process than it does in Trichosurus, so that only a small portion of the neck of the latter is exposed. The residual lumen is narrow and cup-shaped, following the outline of the pars neuralis, from which it is separated by a thin epithelial layer, the pars infundibularis (P.I.), which in most places is only one cell thick. A thin layer of connective tissue lies between the pars infundibularis and the pars neuralis.

In the transverse section of this stage the differentiation of two types of cells in the pars distalis is very well marked, the cytoplasm of the chromophilic cells, which are still few in number, staining a bright, clear

red. In the longitudinal section figured, however, there are few chromophilic cells, and these are not markedly differentiated.

The pars tuberalis forms a thin sheet of much-flattened tubules (P.T.), lying between the diencephalic floor and the pars distalis (P.D.), and invested by a thin layer of connective tissue. A small amount of this section of the pars buccalis has penetrated to the middle line anterior to the hypophysial stalk, but the greater part of it lies laterally thereto. The cellular con-

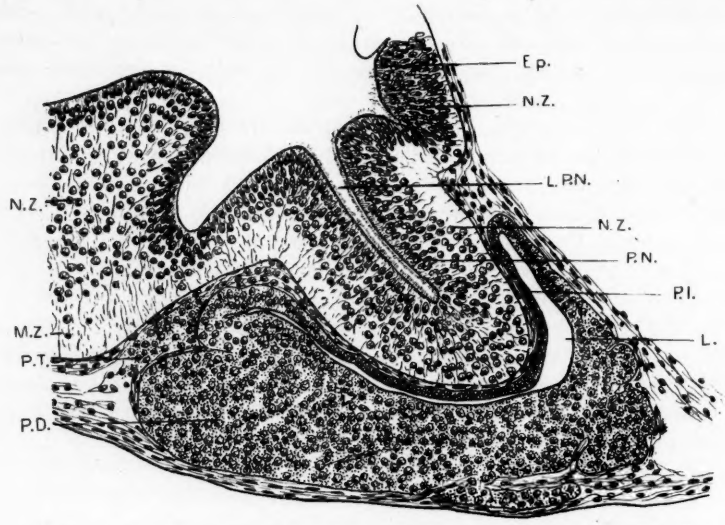

FIG. 40.—Stage H. *Dasyurus viverrinus*. Median longitudinal section through hypophysis. Sl. 3-1-12.

Ep., ependyma; L., lumen; L.P.N., lumen of pars neuralis; M.Z., marginal zone; N.Z., nuclear zone; P.D., pars distalis; P.I., pars infundibularis; P.N., pars neuralis; P.T., pars tuberalis.

nection of the pars tuberalis with the ventral side of the pars distalis is lost, but its origin from the proximal lobe is clear from earlier stages of Dasyurus.

The infundibular process is thick and bluntly pointed, and contains a well-defined, narrow cavity (L.P.N.). The walls of the process contain a large number of cells. In the region of the neck these are restricted to the inner half of the wall, *i.e.* that bordering the lumen, whilst the outer part is exclusively composed of fibres. The cells of the innermost layer constituting the ependyma are apparently ciliated, and are continuous with the ependymal cells lining the brain vesicles. They are not histologically

different from the remaining cells which constitute the nuclear or mantle zone (N.Z.). In the distal half of the infundibular process the nuclei of the mantle zone extend out to the periphery, leaving no distinct marginal zone, though they are less closely packed in this region.

Stage I. *Pouch fœtus, G.L.* 17 *mm., H.L.* 10 *mm.*—The only change which has occurred in the pars buccalis consists in the increase in the number of the chromophilic cells, which are particularly numerous in the posterior portion of the pars distalis.

The infundibular process has thickened, but its cavity still persists. The ependyma cells can be more readily distinguished from the cells of the nuclear zone, and form a layer, several cells in thickness, lining the lumen.

Fibres can be traced from the internal limiting membrane, passing outwards amongst numerous nuclei scattered through the thickness of the wall. In this stage, as in the last, it is only in the neck of the pars neuralis that a definite marginal zone, consisting of fibres only, can be recognised. In this stage, however, the number of cells is less in comparison with the thickness of the wall than in the preceding, and the fibres are correspondingly more conspicuous.

In the transverse series of this stage the lumen of the infundibular process is already obliterated, but in other respects it shows no difference from the longitudinal series.

Stage J. *Pouch fœtus, G.L.* 20 *mm., H.L.* 12·5 *mm.*—The pars buccalis shows no advance on the preceding stage.

The infundibular process (fig. 41), on the other hand, has undergone considerable changes. The whole structure is considerably enlarged, and now has a round, expanded distal portion and a slightly constricted neck. The cavity is obliterated, but its site is indicated by an axial mass of ependymal cells (Ep.). The number of cells in the infundibular process as a whole is relatively, at least, much smaller, so that the pars neuralis now appears to consist of an interlacing mass of fibres with nuclei scattered amongst them. These cells are not restricted to any one portion of the structure, but, apart from the concentration of ependymal cells at the line of closure of the lumen, they are uniformly distributed, so that even in the region of the neck a marginal zone is no longer recognisable. On the other hand, in the region of the tuber cinereum, immediately anterior to the neck of the infundibular process, typical mantle and marginal layers are differentiated.

It thus appears that the infundibular process arises as a diverticulum of the diencephalic floor, whose walls undergo differentiation into ependymal, mantle (nuclear), and marginal zones similar to those of the brain wall.

Subsequently, however, the walls of the pars neuralis undergo modification, becoming more fibrous than those of the brain. As already seen in Trichosurus (Stage XI.), it later undergoes further changes due to the ingrowth of connective tissue and cells of the pars infundibularis.

Perameles nasuta.—Apart from details of no apparent importance, such as the differences in the shape of the hypophysis in some stages, the

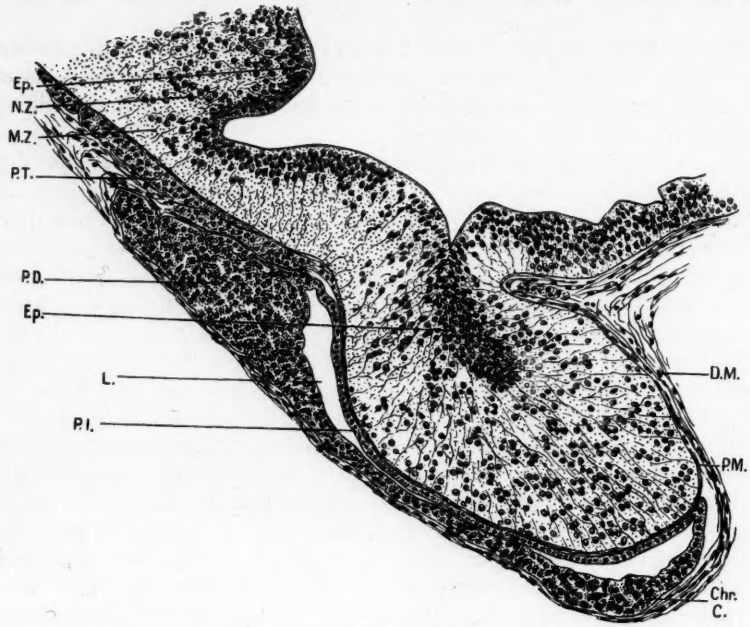

FIG. 41.—Stage J. *Dasyurus viverrinus.* Median longitudinal section through hypophysis. Sl. 1–2–7.

Chr.C., chromophilic cells; D.M., dura mater; Ep., ependyma; L., lumen; M.Z., marginal zone; N.Z., nuclear zone; P.D., pars distalis; P.I., pars infundibularis; P.M., pia mater; P.T., pars tuberalis.

development of the pituitary body in Perameles closely resembles that of Trichosurus. The differentiation of proximal and distal lobes and the process of formation of glandular tissue follows the same course as in Trichosurus.

It is interesting to note that, in spite of the marked development of Seessel's pocket in *Perameles nasuta* (13, VII. 05), Stage IV., described in Section I. of this paper, there is no trace of this structure in any subsequent stage.

The relations of the meninges to the various parts of the hypophysis in a Perameles pouch young of 35 mm. G.L., 18·5 mm. H.L., are precisely the same as in Trichosurus, Stage XI. (p. 212).

Summary and Discussion.

I. *The Premandibular Somites, Prechordal Plate, and the Anterior End of the Notochord.*

It is not within the scope of the present paper to deal in any detail with the literature relating to the premandibular head cavities, which is discussed at greater length in relation to the development of the eye muscles in Marsupials by Elizabeth A. Fraser (12).

That the relatively small and irregular structures described in Section I. of this paper are in reality the precursors of the definitive premandibular head cavities described in later stages by E. A. Fraser (12) is evident from comparison with lower Vertebrates, more especially Selachians and Reptiles. In Selachians (Platt, 42, 43), the premandibular head cavities are structures of considerable size, and are connected with each other by a transverse canal (see fig. 42, Pm.B.). Both the premandibular head cavities and the connecting bridge are derived, according to Platt (42, 43), from an entodermal outgrowth from the fore-gut.

Oppel (40) describes the occurrence of premandibular head cavities and a connecting bridge in *Anguis fragilis*. These originate from a mass of entoderm cells to which he has given the name "præchordal Platte," situated between the wall of the fore-gut and the head of the chorda.

C. E. Johnson (25) describes the premandibular somites in an early stage of Chelydra (3·5 mm.) as consisting of a small group of cells arranged in a radiating manner around a central lumen (*cf.* figs. 3 and 4). These are connected by a bridge, the median portion of which forms part of a mass of cells arising from the anterior wall of the fore-gut. A similar mass of cells has been described as the point of origin of head cavities by Hoffmann (23).

Filatoff (10), Corning (7), Salvi (48), and Dorello (9), on the other hand, describe the origin of the premandibular cavities from the wall of the fore-gut itself.

The embryos of Perameles (Stage I., Section I), Bettongia (Stage II., Section I.), and Macropus (Stage III., Section I.), described above, form a series of stages in which we can trace the origin of a pair of outgrowths clearly corresponding with the premandibular somites of Selachians and Reptiles, arising, as in lower Vertebrates, from a prechordal plate, and connected in Macropus by a transverse bridge.

This prechordal plate is not yet developed in a stage of Perameles preceding the first described in the present paper, but there is present in early stages of Perameles the massive protochordal plate described by Wilson and Hill (63). The protochordal plate from the first shows evidence of active growth power, and gives rise to the pre-oral gut (Seessel's pocket), and to the upper portion of the oral plate. It seems evident that it also gives rise to the prechordal plate in Perameles, for continuity is retained between that structure and the wall of the fore-gut derived from protochordal plate in Stage I. (fig. 1), and again between the prechordal plate and Seessel's pocket in Stage IV. (fig. 6).

The history of the protochordal plate has been fully described in the dog by Bonnet (6), who points out that here it gives rise not only to a portion of oral plate, but also to the "pre-oral entodermal pouch" and to mesoderm. He homologises the "interepithelial cell-mass" of Rex (47) with the protochordal plate, and points out that the difference in the various accounts of the development of the premandibular head cavities refer only to their mode of origin from the "interepithelial cell-mass."

The above account of Perameles agrees closely with that given by Bonnet (6). The pre-oral entodermal pouch of Bonnet (6) and Dorello (9), the interepithelial mass of Rex (47), the præchordal Platte of Oppel (40), the Zwischenplatte of Filatoff (10), as well as the unnamed mass of cells described by Platt (42, 43) and others as the point of origin of premandibular somites, all alike represent derivatives of the protochordal plate. Moreover, as the wall of the anterior angle of the fore-gut is also a derivative of the protochordal plate, the origin of premandibular somites directly from the fore-gut, as described by Corning (7) and Salvi (48), may readily be interpreted on the same lines, for in either case the ultimate source of the premandibular somites and their connecting bridge is the protochordal plate.

Attention may here be drawn to a possible interpretation of the structure described and figured by Selenka in Didelphys (55) under the name of "Gaumentasche." This structure he regards as the branched and hollow anterior end of the chorda. In a later paper (56) he states that he has observed a similar structure in the chick and the duck, as well as other Vertebrates. I have found no trace of such a branched gland as he describes in an embryo of *Didelphys virginiana* (8·5 mm. G.L.) in Prof. Hill's collection which I have examined. Selenka's fig. 16, plate xxx. (55), shows so close a resemblance to the condition described and figured in *Perameles nasuta* (Stages I. and IV., Section I., figs. 1 and 5) as to suggest that the "Gaumentasche" which he observed is nothing more than a prechordal plate in continuity with a well-developed Seessel's pocket.

With regard to the relations of the anterior end of the chorda to the fore-gut and Rathke's pouch, a number of observers have described the apex of the notochord as being in continuity with the hypophysis in birds (Mihalkovics, 33), and in Eutheria (Bonnet, 6; Woerderman, 64; and Miller, 35). This condition is purely secondary, and my own observations lend not the slightest support to the view of Miller that the notochord makes a considerable contribution to the developing hypophysis.

The primitive relation of the anterior end of the chorda is one of continuity with the protochordal plate. The subsequent history can be

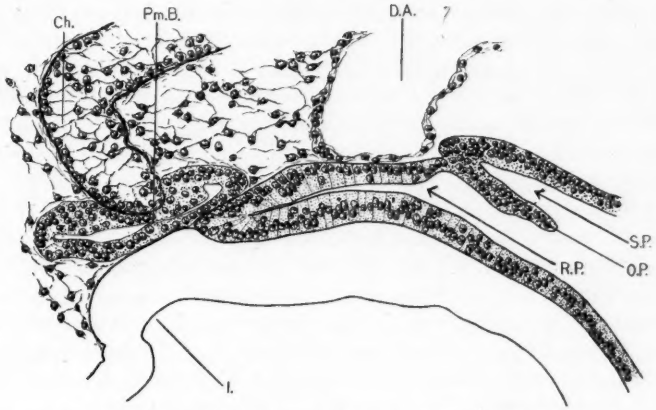

FIG. 42.—*Squalus acanthias* (14 mm. embryo). Median longitudinal section (reconstructed) through the hypophysis and chorda. Sl. 1-4-2-9.

Ch., chorda; D.A., dorsal aorta; I., primitive infundibular recess; O.P., oral plate; Pm.B., bridge connecting premandibular head cavities; R.P., Rathke's pouch; S.P., Seessel's pocket.

clearly followed in stages of Perameles, for, as the various derivatives of the protochordal plate become established, the chorda retains its continuity therewith until we get the condition shown in figs. 5 and 6 in which the notochord is continuous with the prechordal plate and this again with Seessel's pocket. In forms in which a transverse premandibular canal is developed, the continuity between chorda and pre-oral gut is of necessity interrupted, so that the primitive condition is transient. Moreover, the hypophysis at this period grows rapidly backwards, while Seessel's pocket, at the same time, in most Vertebrates degenerates. It will be readily seen that this would produce, in a stage immediately succeeding Perameles, Stage IV. (fig. 5), a condition of contact of Rathke's pouch with the prechordal plate or with a "bridge" connecting the premandibular somites.

This latter condition occurs in Selachians (fig. 42), and is described by van Wijhe (62). In Eutheria, in which neither a definite prechordal plate nor a bridge connecting premandibular somites has been described, the notochord naturally comes into contact with Rathke's pouch, and in some cases—pig, Miller (35), Woerderman (64); dog, Bonnet (6)—there is temporarily established a continuity between the two structures.

II. *Seessel's Pocket* (*Pre-oral Gut*).

In 1877, Seessel (54) first described in the chick a small diverticulum of the gut wall, lying posterior to the hypophysis and in such close contact therewith that its lower concave surface lies exactly on the upper convex surface of the hypophysis. He states that it has a narrow funnel-shaped cavity and a wall of radially placed cylindrical cells, of the same thickness as the hypophysis wall. The reduced remnant of this structure he observed at a later stage as a short diverticulum attached to the duct of the hypophysis.

Seessel's pocket has been described by Nusbaum (39) in the dog as occurring immediately behind a fold which separates it from the hypophysis. In 80 per cent. of the dog embryos examined by Nusbaum, Seessel's pocket comes into close relation with the hypophysis. The lower portion is connected with the pharyngeal epithelium, and contains a small lumen. The distal half breaks up into several cell-groups, one of which passes, in part at least, into the wall of the hypophysis, while the rest of Seessel's pocket disappears completely. Nusbaum regards these facts as evidence that Seessel's pocket and the hypophysis are both parts of one and the same structure, viz. an ancestral communication between the pharynx and the exterior, similar to the unpaired naso-hypophysial duct of Myxinoids.

A portion of pre-oral gut has also been recognised by Bonnet (6) in the dog, and by numbers of other workers in various Vertebrates. Salvi (50), in a detailed study of the pre-oral gut of birds, describes the formation of a succession of "intestinal vertices" of which the tertiary one represents Seessel's pocket. The obliteration of this gives rise to the final "quaternary intestinal vertex." He also describes (48) intimate relations between the pre-oral gut, premandibular somites, and the hypophysis, but does not find any contribution from the entoderm of Seessel's pocket to the hypophysis.

This participation of the entoderm of Seessel's pocket in the formation of Rathke's pouch has also been described by von Kupffer (30) and Saint-Remy (52).

In the Marsupials which I have examined, Seessel's pocket is of common occurrence. In Dasyurus it is very small and variable in its relations,

(*cf.* Stage III. of *Dasyurus viverrinus*, Section I. of this paper), but in this species, as the hypophysis deepens and closes, Seessel's pocket disappears, leaving no trace.

In Trichosurus, Seessel's pocket bears relations to the hypophysis similar to those described by Seessel for the chick. It forms a small conical diverticulum, separated from Rathke's pouch by a remnant of oral plate; and, as the posterior end of the hypophysis is slightly bilobed, Seessel's pocket lies between the lobes. (Trichosurus, Stage I.) In the process of narrowing of the mouth of Rathke's pouch, the posterior point of constriction is situated behind the opening of Seessel's pocket (fig. 17), so that that structure becomes included in the hypophysial duct and forms for a time a small pocket-like diverticulum on the posterior side of the duct. This subsequently disappears, and it cannot definitely be said that it contributes actively to the formation of the hypophysis, for it is merely continuous with the duct, which is itself destined to disappear. It is perfectly clear, however, that the insertion of the oral plate, which marks the point of junction of ectoderm and entoderm, comes to be situated within the tissues of the hypophysis, which accordingly cannot be regarded as of exclusively ectodermal origin.

In Perameles a well-developed Seessel's pocket is present in one stage (*P. nasuta*, Stage IV. of Section I.). It arises undoubtedly from the region of the fore-gut derived from the protochordal plate, and is directly continuous with the remnant of the prechordal plate. In subsequent stages, however, all trace of Seessel's pocket has disappeared.

In Phascolarctos and Phascolomys we find the most remarkable development of Seessel's pocket. In Phascolarctos, Stage III., it appears at first sight to form a third median lobe of the bilobed caudal portion of the hypophysis, and its identity is only clear from the fact that it arises posterior to the oral plate. The constriction of Rathke's pouch then occurs in such a manner that Seessel's pocket is included in the hypophysis, and, instead of degenerating as it does in other cases, it persists as a portion of the pars buccalis. Up to a relatively late stage it is recognisable as a flattened vesicle lying on the ventral surface of the hypophysis, and in several embryos its original relations to the caudal bifid extremity of Rathke's pouch are retained, so that sections through the hinder end of the hypophysis in the last stage of Phascolarctos described above bear a very close resemblance to those of the third stage (fig. 34). In some cases Seessel's pocket has the appearance of being an integral part of the hypophysis (fig. 38), whereas in other cases its walls are completely separated by connective tissue from the rest of the pars buccalis and it retains to some extent its own identity. In later stages, however, it

appears simply as a slightly differentiated tubule or lobe of the hypophysis.

In Phascolomys, again, we find a well-developed Seessel's pocket which, like that of Phascolarctos, becomes included in the buccal portion of the hypophysis. In early stages of Phascolomys (fig. 39) Seessel's pocket forms a long, conical diverticulum, opening on to the posterior face of the hypophysial duct. The walls are slightly less regular than those of Rathke's pouch, and its cells are distinguishable from those of the hypophysis by reason of their greater staining capacity.

We have thus undoubted evidence that Seessel's pocket in at least two Marsupials (*Phascolarctos cinereus* and *Phascolomys mitchelli*) actually enters into the composition of the pars buccalis of the pituitary body, whilst in Trichosurus a doubtful amount of entoderm is included in the hypophysis.

Professor Hill has drawn my attention to the fact that in an Echidna embryo in his collection there is a well-developed Seessel's pocket. From Professor Hill's graphic reconstruction of this embryo it is clear that Rathke's pouch has just formed; the oral plate is ruptured, and behind it is a conical diverticulum, slightly longer than the hypophysis. Whether this structure subsequently degenerates in Echidna or forms part of the hypophysis is unknown. The condition in the above-mentioned embryo closely resembles that in Phascolarctos, Stage II., 7·5 mm., in which, however, the hypophysis is further advanced and is accordingly slightly longer than Seessel's pocket.

The occurrence of such a well-developed Seessel's pocket in Monotremes and Marsupials and its inclusion in the hypophysis in Phascolarctos and Phascolomys is remarkable, and its significance is uncertain. It must be admitted as a possibility that the inclusion of the pre-oral gut in the pars buccalis indicates nothing more than a slight variation from the normal Vertebrate method of closure of the hypophysial pouch. Further observations are necessary to prove how frequently the phenomenon occurs in other groups of Vertebrates.

In connection with the discussion as to the fate of Seessel's pocket, it may be well to make a brief reference to the pharygneal bursa, a structure of doubtful significance, which has been identified with Seessel's pocket by some workers (Meyer). This structure was first described by A. J. C. Mayer (31) in 1840, and has since been discussed by Killian (28), Grünwald (17), Meyer (32), Huber (24), and others. Huber, in a full discussion on the subject, decides against Meyer's theory that the pharyngeal bursa is merely a persistent Seessel's pocket, on the ground that the two structures are separated by almost the whole length of the future pharyngeal vault;

and the same objection applies to the suggestion that the pharyngeal bursa is a persistent hypophysial duct.

I have not been able to find any trace of a pharyngeal bursa in any Marsupial embryo which I have studied; but if such a bursa is present at any stage in Marsupials, it cannot be derived from Seessel's pocket, as that structure either degenerates completely or becomes part of the hypophysis; neither can it represent a persistent hypophysial duct, as that retains for some time its relations to the hypophysis and then disappears completely.

III. *The Formation of Rathke's Pouch.*

An excellent historical note on the pituitary body is given by Herring (22) in a recent paper, and it is unnecessary to recapitulate here the many different views that have been held as to the ontogenetic and phylogenetic origin of the hypophysis. Rathke (46), in 1838, was the first to describe the origin of the anterior lobe of the pituitary from a pouch-like ingrowth. Subsequent work has established the ectodermal origin of this structure beyond question.

In early stages of Dasyurus described above, we see the exact relations of Rathke's pouch to the fore-gut and oral plate. In Stages I. and II. the oral plate (figs. 8 and 9, O.P.) is still complete, and in the former there is as yet no indication of the formation of the hypophysis. In Stage II. no definite invagination has taken place, but the hypophysial epithelium is differentiated, and this differentiation affects a small portion of the ectoderm of the oral plate. In the next stage the oral plate is ruptured (fig. 10), but a considerable remnant of it persists. Instead of lying, as it does in the preceding stage (fig. 9), in approximately the same line with the ectoderm of the head, it has become bent forwards so as to form an acute angle therewith. The wall of the fore-gut, which in Stage II. lies in contact with the brain floor, has ceased to do so in Stage III., and a mass of cells, possibly representing a head somite, lies above it (figs. 10 and 11). The modified stretch of epithelium now forms a shallow pouch with its dorsal wall pressed closely against the brain floor. It is evident that the apex of the pouch has grown actively backwards, for in Stage II. (fig. 9) it lies anterior to the infundibular depression, whilst in Stage III. it lies immediately below it. The posterior limitation of the pouch is brought about partly by the backward growth of this apex, and partly, as stated by Mihalkovics (33) and Kraushaar (29), by the forward bending of the oral plate. This movement of the oral plate does not, however, appear to be a purely mechanical result of its rupture, for in *Perameles nasuta* (Stage IV.), in which the oral plate is still complete, there is a

distinct forward projection thereof, close to its dorsal insertion (fig. 5, P.), and this projection forms the posterior wall of Rathke's pouch. The anterior and lateral folds limiting the pouch are simply the result of the active growth of the epithelium of the pouch. Lying as it does with one wall in close contact with the brain, the natural result of active growth and division of the cells is firstly to increase the area in contact with the brain, and secondly to produce round this area folds, or lips, thus converting the structure into a shallow pouch. Stage III. of Dasyurus (fig. 12) shows a further result of this growth in the deepening of the pouch posteriorly.

That the chorda does not in Marsupials play a mechanical role in drawing Rathke's pouch inwards is self-evident from the fact that it stops some way behind the hypophysis in most cases, and is never in actual contact therewith.

As Herring (22) remarks, the close contact between the hypophysial epithelium and the infundibular depression in these early stages is doubtless of importance in bringing about the development of a definite pouch. In most of the early stages there is evidence of very active growth at the lateral angles of the pouch (fig. 7), and it is clear that rapid growth at these points will tend of itself to bring about a deepening of the pouch.

The narrowing of the mouth of the pouch requires a different explanation. Müller (36) put forward the theory that this was due to the pressure of the internal carotid arteries. Mihalkovics (33) and Kraushaar (29) both regard it as due to the development of the primordium of the skull. In Marsupials there are no blood-vessels in a position to cause the narrowing of the mouth of the pouch, and, as far as it seems possible to give any explanation of this phase of development, that given by Mihalkovics and Kraushaar is probably correct, for the narrowing of the opening of the pouch and its final reduction to a slender duct occur contemporaneously with the condensation of the mesenchyme which ushers in the formation of the cartilage of the skull.

The appearances of transverse sections through Rathke's pouch in early stages, such as are shown in figs. 7 and 30, are exceedingly suggestive of a bilobed origin of the hypophysis; whilst in Stage I. of Phascolarctos the condition is even more marked, the epithelium in the middle line being remarkably thin. The activity of the cells of the lateral angles of the pouch is indicated, in most of the early stages which I have examined, by such appearances as are shown in fig. 7. Moreover, these lateral angles tend to be prolonged backwards beyond the median portion of the pouch, thus giving rise to a distinctly bilobed caudal extremity. In Trichosurus, and more especially in Phascolarctos, this branching of the pouch may be

due to the presence of a median Seessel's pocket, indenting the posterior wall of Rathke's pouch. In Trichosurus the caudal bifurcation persists and even becomes more marked after Seessel's pocket has become a mere remnant attached to the duct, and the conical infundibular process, which is just appearing, lies between the two halves.

It is impossible to say at present whether this bilobed condition indicates the origin of Rathke's pouch from a structure consisting of two symmetrical portions. On the whole, it seems more probable that it is merely due to three independent factors, viz. active growth and multiplication of the cells at the angles of the pouch, the pressure of Seessel's pocket on the middle line of the posterior wall of the pouch, and the subsequent protrusion of the infundibular process into the same position.

It may be noted that Gaupp (13) and Salvi (48) have described a threefold origin of the hypophysis in Reptiles, but the lateral lobes in this case probably represent nothing more than an early establishment of the primordia of the pars tuberalis.

IV. *The Later Development of the Hypophysis cerebri.*

The development of the hypophysis subsequent to the establishment of Rathke's pouch consists in the outgrowth and differentiation of the infundibular process, and in the conversion of the simple thin-walled buccal pouch into the various regions characteristic of the pars buccalis of the adult, viz. the solid glandular pars distalis, the pars infundibularis, and the pars tuberalis.

(*a*) *The Development of the Pars buccalis.*

1. *Development of the Pars juxta-neuralis.*—The separation of the primordium of the pars tuberalis occurs in Marsupials at a very early stage, and this fact gives confirmation to the view of Tilney (59) that the pars tuberalis and pars infundibularis constitute two distinct morphological elements in the pars juxta-neuralis.

According to Tilney (59), the pars tuberalis in the adult cat, dog, rabbit, rat, sheep, and fowl "is moulded to the base of the brain in such a manner that the saccular eminence of the tuber cinereum rests in it as one saucer in another" (Tilney, 59, p. 263), whilst a median aperture in the pars tuberalis admits of the passage of the infundibular process. With regard to its ontogeny, he describes in a 14-mm. cat embryo the appearance of a pair of processes from the lateral borders of the dorsal surface of the buccal pouch in the region where the neck of the pouch joins the body. These are destined to form the pars tuberalis, and he accordingly calls them tuberal

processes. They grow up towards the brain, and also extend both posteriorly and anteriorly, to fuse eventually and form a continuous structure lying between the tuber cinereum and the pars distalis. In the chick of 5 days, 20 hours he describes the origin of tuberal processes "near the cephalic pole of the body of the pituitary anlage."

Although Tilney alone has clearly recognised both the origin and fate of this portion of the hypophysis, it seems probable that certain structures described by other authors may prove to be identical with it. Thus Mihalkovics (33) and Kraushaar (29) have described the development of a solid process arising from the lower end of the hypophysial sac and growing forwards towards the optic chiasma. Salzer (51) has given special attention to the subject, and finds that in the pig there is an epithelial thickening which corresponds to the process described by Mihalkovics (33) in the rabbit, and by Kraushaar (29) in the mouse. This sends forwards "towards the chiasma" a process consisting of glandular substance. Salzer states also that he finds a similar anterior process in the guinea-pig.

Herring (21 and 22) describes "a tongue-like process of the pars intermedia" in the cat and monkey, and from his figures it seems probable that this structure is the anterior portion of the pars tuberalis. (Compare figs. 2 and 5 of Herring (21) with Tilney's (59) longitudinal sections, figs. 1, 2, 5, 7, 9, etc.) With regard to the development of this portion, Herring (22) states that the neck of the hypophysial sac retains a tubular character for some time and becomes somewhat convoluted. "One of these convolutions applies itself to the under surface of the brain and gives rise to the tongue-like process which extends forwards from the anterior lobe towards the optic chiasma": Herring (22, p. 171).

Baumgartner (4), in a description of the development of the hypophysis in turtles, describes the presence in an early stage (5-mm. embryo) of a main pouch and two lateral buds. The free ends of these lateral buds grow forwards and dorsalwards, and later their distal portions become wing-like and extend forwards beneath the brain floor, whilst their proximal parts lateral to the anterior lobe are crescentic in transverse section. In the newborn animals the lateral lobes have fused across the median line, whilst their crescentic, proximal portions are united by outgrowths of their free edges both dorsally and ventrally around the "anterior lobe," so that this latter is enveloped by the layer so formed. This description probably refers to a pars tuberalis such as is described by Tilney (59), and having an origin similar to that described for Marsupials.

It may further be noted that Baumgartner's description affords an explanation of the threefold origin of the hypophysis decribed by Gaupp

(13) and Salvi (48) in Reptiles. Baumgartner finds a median pouch developed first, followed by two lateral buds. Gaupp (13) similarly describes three invaginations, the two lateral ones forming elongated slit-like depressions separated from the median one by fairly considerable folds in which lie a pair of veins (*cf.* fig. 33). In later development, the three invaginations deepen and become simultaneously nipped off from the mucous membrane. The lateral lobes separate from the median and may degenerate, but Gaupp finds in almost adult lizards two groups of cells, apparently derived therefrom, actually embedded in the walls of the diencephalon. These groups of cells may represent a displaced pars tuberalis.

Salvi (48) describes similar lateral primordia in Reptiles, but does not trace their subsequent history. On the ground of a connexion between these structures and the premandibular somites, he regards the lateral pits as equivalent to the ectodermal invaginations of a pair of gill slits. The development of the premandibular somites in Marsupials lends no support to the theory that they represent gill pouches, nor is there any evidence in this group in support of Salvi's interpretation of the significance of the lateral pits of Gaupp.

Comparing Gaupp's (13) and Salvi's (48) accounts with that of Baumgartner (4), and with the mode of development of the pars tuberalis in Marsupials, it seems probable that the threefold origin described by Gaupp and Salvi may prove to represent an early differentiation of the primordium of the pars tuberalis.

The development of the pars tuberalis in Marsupials is perfectly clear. In quite early stages the portion of Rathke's pouch lying posterior to the duct becomes subdivided into two lobes, which are respectively distal and proximal in relation to the hypophysial duct, and are separated from each other by a horizontal constriction. While the distal lobe thickens and forms the glandular tissue of the pars buccalis as well as the pars infundibularis, the proximal lobe remains thin-walled. It becomes drawn out laterally, and early becomes crescentic in transverse sections. (Compare figs. 18, 20, 21, and 26.) Its lateral borders enlarge and curve up towards the dorsal side of the pars buccalis (figs. 26, 37). These wing-like structures are prolonged anteriorly considerably beyond the main body of the proximal lobe. In subsequent stages the median portion of this lobe becomes greatly reduced, loses its lumen, and fuses with the ventral surface of the distal lobe, whilst the enlarged lateral portions grow up towards the brain floor. Finally they branch and form a collection of flattened tubules which, increasing greatly in number, extend first anteriorly and meet and fuse in the middle line in front of the infundibular process,

whilst later they penetrate to the caudal side of that structure and thus come to form a complete ring around it.

Up to the latest stage which I have studied (Trichosurus, Stage XI., fig. 29), the pars tuberalis consists of hollow, flattened tubules with thin walls for the most part only one cell in thickness, and consisting of cubical epithelial cells. No variation in staining capacity is evident in these cells.

From the above summary it becomes clear that the pars tuberalis takes its origin at a very early stage from Rathke's pouch. In Reptiles, if my interpretation of Baumgartner's and Gaupp's descriptions is correct, it arises from a pair of hollow outgrowths which are at first separate from the main median hypophysial invagination. The three primordia become simultaneously nipped off from the buccal ectoderm, thus acquiring a common duct. In the Marsupials, the narrowing of the mouth of the pouch takes place before the differentiation of the tuberal primordium, but this is still a hollow outgrowth whose subsequent history clearly shows its homology with the lateral invaginations described by Baumgartner (4). In the Eutheria, according to Tilney (59), the pars tuberalis is derived from a pair of solid processes arising from the point of junction of the neck and body of the hypophysis, this being also the position of the proximal (tuberal) lobe in Marsupials.

The development of the pars infundibularis shows no point of special interest. The postero-dorsal wall of Rathke's pouch represents the primordium of this portion. Unlike the rest of the distal lobe, it never thickens markedly, but on the contrary, as development proceeds, becomes reduced to a thin and very regular layer of epithelium. The infundibular process as it grows downwards indents it from above, and during the growth of the hypophysis as a whole the pars infundibularis spreads round in all directions, so that it eventually comes to cover the infundibular process on its anterior and lateral sides, and to a certain and variable extent on its posterior face. It is noticeable that in the Marsupials the thin epithelium of the pars infundibularis forms not only the layer in contact with the pars neuralis, but also extends beyond this, forming the ventral wall of the anterior and posterior angles of the residual lumen (*cf.* fig. 27), and the dorsal wall of its lateral horns (fig. 28).

With regard to the time of penetration of connective tissue between the buccal and neural portions of the hypophysis, various statements have been made. As noted by Herring (22) and Salzer (51), in the initial stages these two parts are in intimate contact. In a Trichosurus embryo of 8·5 mm. G.L. (Stage V.), connective tissue has penetrated between the primordia of the pars neuralis and the pars buccalis. This connective

tissue is derived from the pia mater, and not, as would be supposed from Stendell's (57) description and figure (fig. 17), from the dura mater.

In the final stages of development (Trichosurus, Stage XI.) some of the cells of the pars infundibularis become carried by growth and penetration of the connective tissue into the substance of the pars neuralis, while the remainder form a thin epithelial layer surrounding that structure.

2. *Development of the Pars distalis.*—In the Marsupials which I have studied, two methods of conversion of the walls of Rathke's pouch into the glandular pars distalis may be observed. Of these methods, that observed in Phascolarctos is probably the more primitive, and will accordingly be dealt with first, that of Trichosurus being more specialised. In both cases the cells of the walls of the distal lobe of Rathke's pouch multiply freely except in the region of contact with the developing infundibular process. In both cases also there is produced from the posterior half of the pars buccalis a pair of large, dorso-lateral outgrowths into which a narrow cleft-like lumen extends. (*Cf.* fig. 22, in which, however, the actual section figured passes not through the lumen but through the solid wall.) In Phascolarctos capillaries supplying the pars distalis enter by the ventral cleft between this lateral wing-like process and the median lobe. I have not been able to ascertain with certainty whether this is the case in Trichosurus or not, though a large amount of connective tissue undoubtedly penetrates at these points. It therefore seems possible that the separation of these lobes by a pair of ventral clefts merely serves to afford a point of entry for connective tissue and blood-vessels.

In Phascolarctos, the rapid multiplication of the cells of the walls of Rathke's pouch results in the outgrowth of numerous processes from the outer surfaces of the walls. These are at first short and rounded, but soon become longer; their extremities enlarge and in some cases acquire a lumen (*cf.* fig. 36). They increase rapidly in number, so that the pars distalis comes to consist of a mass of tubules and cell cords, separated from one another by connective tissue which, from the nature of the process of development, inevitably becomes included in the walls.

Although in Phascolarctos, Stage VIII. and in the following stages, as well as in Phascolomys, the very rich vascularity of the pars buccalis is noticeable, there is no indication of sinusoidal development such as Herring (22) describes in the pig. In earlier stages there are blood-vessels lying in close proximity to Rathke's pouch, but these do not penetrate until Stage V., and at no stage is there any indication of the processes from the walls of Rathke's pouch growing into the blood-vessels and pushing the endothelial walls before them as described by Herring (22). On the contrary, several definite points of penetration of the capillaries into the substance of

the pars distalis can be recognised, viz. the ventro-lateral clefts as already mentioned and the posterior wall of the pars distalis.

It seems, therefore, that in Phascolarctos there occurs, contemporaneously with the outgrowth of processes from the walls, a certain amount of ingrowth of connective tissue, and more especially of blood-vessels.

Salzer (51) describes a similar condition in the pig, and draws attention to the fact, which is true also of Phascolarctos, that the lumina of the tubules arise entirely independently of the main lumen. Mihalkovics (33) in the chick, and Kraushaar (29) in the mouse, both describe the formation of tubules simply by outgrowth from the wall of the buccal pouch.

In Trichosurus, on the other hand, the walls of Rathke's pouch thicken considerably, so that the lumen is much reduced; but up to Stage VII. the walls retain their original compact form, with a regular, unbroken outline. The process of "tubule" formation then begins, and is ushered in by the ingrowth of connective tissue strands at a number of points. The cells of the wall then gradually become grouped so as to form lobules and cell-cords, but in no stage in Trichosurus do these acquire a lumen. By further ingrowth of connective tissue, and by a process of grouping and rearranging of the cells, the pars distalis of Trichosurus acquires a glandular structure. As might be expected from the difference in the mode of development, the pars distalis in Trichosurus is throughout its history a very much more compact structure than that of Phascolarctos.

A similar process of gland formation by ingrowth of connective tissue was described by J. Müller (36) for the pig; but, according to Salzer's (51) very full and careful description, outgrowths of processes from the wall also play a large part in the development of the hypophysis of this Mammal.

It would be natural to assume that the primitive mode of elaboration of a glandular structure such as the pars distalis is that of the formation of outgrowths, probably hollow, from the walls of a simple pouch. The tubules thus formed would, as they increase in number, become pressed together until they constitute a relatively compact gland. In the adult hypophysis in Mammals the tubular structure is almost entirely lost (*cf.* Herring, 22), and there seems to be a tendency to omit in development the stage of formation of hollow outgrowths.

In the Mammalia both the process of outgrowth and that of penetration of connective tissue occur contemporaneously, and the Marsupials which I have studied form a well-graduated series in this respect. In Phascolarctos and Phascolomys the process of formation of outgrowths from the walls of Rathke's pouch undoubtedly plays a markedly preponderating part in development, while ingrowth of connective tissue occurs to a relatively slight extent. In early stages in Dasyurus, outgrowths form on the walls,

but they are neither so numerous nor so long as those in Phascolarctos and Phascolomys. In Trichosurus and Perameles outgrowths of the walls play but a very small part, the adult condition of compactness being attained by a far less circuitous method by direct increase in thickness and by contemporaneous rearrangement of the constituent cells of the walls as cell-cords or lobules.

In this connection it may be noted that whilst in Stage V. of Phascolarctos the bulk of the pars distalis consists of definite tubules, the lumina of these is lost for the most part, if not entirely, in later stages.

Embryological evidence thus agrees with the facts of comparative anatomy, for the anterior lobe in lower Vertebrates consists simply of a greater or less number of branching tubules (Stendell, 57, figs. 63, 65, 66), and we may conclude that the pars buccalis of the Mammals also arose as a branched tubular gland which in the course of evolution became more and more compact until it has in some cases lost, even in ontogeny, all trace of the process by which it has developed.

3. *Histological Differentiation of the Pars distalis.*—The final stage in the development of the pars distalis is the process of histological differentiation. In embryological material not stained for special histology, it is naturally impossible to follow this process in great detail, and it was not my original attention to deal with this subject at all. It may, however, be noted that in later stages in all the types examined the cells of the pars distalis exhibit a very conspicuous differential staining capacity (see figs. 27, 28, 29, 40, and 41). The bulk of the pars distalis in these stages consists of cells with oval or spherical nuclei and cytoplasm which stains a typical hæmatoxylin blue. Amongst these occur a few cells with spherical nuclei and cytoplasm which stains bright red. These two types of cells appear to represent respectively the "chromophobic" and "chromophilic" cells described by Flesch (11) and referred to by Herring (21). Herring (*loc. cit.*) himself describes three types of cells: one small and non-granular, the second larger, with granulated cytoplasm, and thirdly, the deeply staining type. I have not observed any cells which correspond with this second granular type, and merely record the occurrence of the chromophilic cells for the purpose of indicating the stage at which they first appear, viz. in Trichosurus, Stage X. (11 mm. H.L.); Phascolarctos, Stage IX. (9·5 mm. H.L.); Dasyurus, Stage H. (13·5 mm. G.L.). It may also be noted that in all the cases in which these chromophilic cells can be observed they are most numerous in the posterior portion of the pars distalis.

Neither the time of appearance of these cells nor their mode of origin, scattered as they are in the substance of the hypophysis, nor any other facts in development in Marsupials, lend any support to the view of Miller

(35) that the existence of two histologically distinct types of cells in the "anterior lobe" is due to the origin of the one group from ectoderm and the other from entoderm (head of the notochord).

The Fate of the Lumen.—With increase of thickness of the walls of the buccal pouch, the lumen naturally becomes reduced, and in the course of reduction it passes through a variety of forms which do not seem of sufficient importance to justify a detailed description. Two distinct portions of the lumen persist up to Stage X. of Trichosurus: one forming the cup-shaped residual lumen surrounding the pars neuralis; the second, a small isolated cleft on the ventral side of the pars distalis (fig. 27, Lm.P.L.), representing the last trace of the median lumen of the proximal (tuberal) lobe of earlier stages. This small cleft subsequently disappears, whilst the main cavity persists in a pouch fœtus of 4 cm. G.L. (Stage XI.) as a cup-shaped residual lumen.

(*b*) *Development of the Pars neuralis.*

In early stages of development of the brain, prior to closure, a rounded depression of the floor of the diencephalon occurs. This represents the primitive infundibular depression, and it is from the posterior angle of this that the infundibular process grows out. As already stated, I am unable at present to describe the process of development of the diencephalic floor or to identify with certainty the post-chiasmatic and post-infundibular recesses and eminences described by Tilney (60), and the development of the infundibular process is so closely related to that of the diencephalic floor that it is impossible to discuss the former satisfactorily in the absence of definite knowledge of the latter. A few points may, however, be noted.

The infundibular process itself arises as a short, conical or rounded hollow outgrowth from the diencephalic floor, and its walls for a considerable time retain the primitive character of the brain-wall in early stages of its development. Subsequently its cavity becomes reduced and the walls show some indication of differentiation into the three zones, ependymal, mantle (or nuclear), and marginal, characteristic of the developing brain-wall. Complete differentiation is, however, restricted to the neck of the pars neuralis, while in the distal portion cells are scattered throughout the substance of the wall, leaving no specialised marginal zone. The substance of the wall in this stage is traversed by fine fibres, probably both ependymal and neuroglial. In later stages the infundibular process enlarges considerably and its lumen becomes obliterated. The walls undergo several changes, the cells become fewer, the fibres much more conspicuous; and in the last stage which I have observed,

the connective tissue has penetrated to a considerable extent into the substance of the pars neuralis, carrying with it a few of the cells of the pars infundibularis.

V. *Note on the Relation of the Meninges to the Parts of the Hypophysis cerebri.*

In both Trichosurus and Perameles it is possible in late stages to observe the relations of the meninges to the parts of the hypophysis, and in both these types the pia mater completely invests the pars neuralis and also the pars tuberalis (fig. 13, P.M.). This statement differs from the account and diagram (fig. 17) of Stendell (57), according to which the pia mater is perforated by the pars neuralis, while the dura mater passes between the pars neuralis and the pars infundibularis. In the forms which I have examined, the dura mater constitutes a connective tissue capsule, the greater part of it passing ventral to the whole of the pituitary, while a thinner layer passes over the dorsal surface of the pars buccalis but thins out considerably as it approaches the hypophysial stalk, and is not continued between the pars neuralis and the pars infundibularis (see fig. 13). In Marsupials the pia mater does not end, as described by Stendell (57) for Vertebrates generally, at the point of origin of the infundibular process, but penetrates between this latter and the pars infundibularis.

Final Summary.

1. In Bettongia, Macropus, Perameles, and Trichosurus there is present a pair of head cavities whose early relations and subsequent history (see Elizabeth A. Fraser (12)) show them to be premandibular somites. The origin of these structures has been traced only in Perameles, in which they arise from a prechordal plate which represents a derivative of the antero-dorsal wall of the fore-gut, which is formed from the protochordal plate.

2. A well-developed Seessel's pocket (pre-oral gut) occurs in some Marsupials, and in *Phascolarctos cinereus* and *Phascolomys mitchelli* forms a constituent part of the hypophysis.

3. The primitive relation of the tip of the notochord is one of continuity with the protochordal plate, and in Perameles continuity is retained between the chorda and the derivatives of the protochordal plate (prechordal plate and Seessel's pocket). As a secondary condition, continuity may be established between the chorda and the hypophysis.

4. The development of Rathke's pouch is due to rapid growth of the

differentiated epithelium of the hypophysial angle, and not to any mechanical power exercised by the chorda or any other structures.

5. From Rathke's pouch in Marsupials there arises a proximal lobe, at the point of junction of the duct with the body of the pouch. This forms the pars tuberalis of the adult pituitary body.

6. The glandular structure of the pars distalis (anterior lobe) of the adult is produced either by outgrowth of processes from the walls of Rathke's pouch or by ingrowth of connective tissue into the thickened walls of that structure.

7. Two types of cells, "chromophilic" and "chromophobic," are differentiated *in situ* in the pars buccalis before the adult condition is fully reached.

8. The pars neuralis arises as a hollow conical outgrowth of the diencephalic floor. It is gradually transformed into a solid, swollen lobe, and is then penetrated by connective tissue.

Addendum.

Since the completion of the above, a paper has appeared on the development of the hypophysis in Reptiles by Baumgartner (*Journal of Morphology*, vol. xxviii., No. 1, Dec. 1916), who describes the origin of the pars tuberalis in a considerable number of Reptiles from lateral buds such as are described by Gaupp (13), and by Baumgartner (4) in an earlier paper. This is in agreement with the interpretation given above, according to which the lateral buds described in Reptiles are homologous with the proximal lobe found in early stages in Marsupials.

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THE ARTERIES OF THE PONS AND MEDULLA OBLONGATA: PART III.[1]

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PART III.

THE CLINICAL APPLICATION OF PARTS I. AND II.

IT is not within the scope of this thesis to consider fully the theoretical "vascular" etiology which has been proposed for so many cerebral and spinal diseases of obscure origin. The striking correspondence in size and position between the distribution of certain arteries and the areas of sclerosis in several diseases is extremely significant and has been remarked upon by many writers. The localisation of acute anterior poliomyelitis to the distribution of the anterior spinal, which has been observed by Marie (95), Goldscheider (63), Dauber (42). and Seimerlung (122), and cases of posterior sclerosis which have marked out the area supplied by the posterior spinal, as in Buzzard's (31) case, are particularly interesting examples, which at least suggest the possibility of the vascular origin of many nervous diseases whose etiology is difficult to determine. The close relationship between the patches of sclerosis in disseminated sclerosis (or myelitis) and the distribution of spinal blood-vessels has been repeatedly referred to: a typical illustration was reported by Dreschfeld (51).

Williamson (154) and more recently Starr (132) have reviewed fully the relation of nervous diseases to the distribution and lesions of the cerebral and spinal blood-vessels, and reference to their papers shows that greater anatomical knowledge of the nutrient vessels and more extended pathological examinations of the diseased tissues are necessary, if the vexed question of etiology is to be decided. Attention will be briefly directed to this subject again on a later page.

The applied anatomy dependent upon the investigations described in the preceding pages may be most concisely divided into the following parts:—

I. Occlusion of { (A) the main arterial trunks. (B) the small bulbar or pontine branches.

II. The significance of the neuro-vascular relationships.

[1] Continued from *Journ. of Anat. and Phys.*, 1916, vol. l., p. 255.

I. General.

(A) *Occlusion of the Main Arterial Trunks.*

The two exciting causes of occlusion of the large vessels are thrombosis and embolism, and certain of the anatomical arrangements predispose to one or the other. The lesions produced by occlusion only form one section of the elaborate classification of bulbar palsies suggested by Batten (12), but a more perfect anatomical knowledge assists in eliminating many of the recognised difficulties experienced in an endeavour to make a differential diagnosis between the various sections.

Trousseau (143) and Duménil (53) were the first to describe and recognise labio-glosso-laryngeal paralysis as a definite clinical entity, and since their time our knowledge has steadily increased, although it is still very incomplete. Emboli are liable to be arrested:—

1. Most frequently in branches which arise, more or less, in the direct line of the parent vessel. Hughlings Jackson (76) was the first to show that the middle cerebral, being "more directly in the way of strain from the heart," was "plugged" more constantly than any other cerebral artery.

Huret (78) indicated that the *left* vertebral exhibited a greater disposition to embolism than the right, on account of its more direct position in the axis of the flow from the left ventricle. Many anatomists have stated that the left common carotid is more in the line of the ascending aorta than the innominate.

As an embolus usually consists of a detached vegetation from the mitral or aortic valves (Savelieu (119) found embolism associated with heart disease in 89 per cent.), the gross anatomical arrangement of the vessels suggests that embolism should be found most frequently on the left side in both the carotid and vertebral systems. Furthermore, the size and anatomical position of the left common carotid would predispose to its occlusion by an embolus more frequently than the left vertebral.

Clinical statistics support these anatomical conclusions. Jeanin (80) only succeeded in finding 19 cases of embolism of the right side in the literature, but more recently Jones (81) traced 639 cases of embolism, all verified by autopsies, of which 332 were on the left and 307 on the right.

In 372 cases of thrombosis the latter discovered 196 on the left and 176 on the right.

2. In the region of the bifurcation of a vessel, as there is usually a

reduction in calibre at the site of division. This is well illustrated by the basilar artery, which is most frequently obstructed by an embolus at the point where it bifurcates to form the two posterior cerebral arteries, although it is necessary to point out that embolism of this vessel is rare.

3. At any point where there is a sudden diminution in the diameter of an artery. This will be clearly demonstrated subsequently by the vertebral artery.

4. Naturally more frequently in the smaller arteries. Embolism of the basilar is rare, because fragments which have passed uninterruptedly through the vertebral would scarcely be likely to become lodged in the former artery, which is larger than the latter.

Another anatomical factor which influences the clinical result of arterial obstruction is the possibility of the maintenance of the circulation in cases of obstruction by the normal anastomoses.

The circle of Willis is undoubtedly the most important of these. It has been seen that the posterior communicating arteries connect the carotid and vertebral systems, and furthermore that the anterior communicating forms a junction between the cerebral arteries of the two sides, although under normal circumstances the circulation of the two hemispheres may be described as practically distinct. From this it is not difficult to realise that this arterial circle, when complete, may compensate for complete occlusion of the internal carotid. This explains the very frequent absence of symptoms, or transient hemiplegia, which follows ligature of the internal carotid, and the clinical significance of absence (4 per cent. on right side and 3 per cent. on the left) or diminutive size of the posterior communicating artery, which may cause permanent hemiplegia when the internal carotid is obstructed. Alexander (4) introduced ligature of the vertebral (even both) as a treatment for certain diseases of the spinal cord, and stated there was an improvement in the majority of the cases; but what is more interesting in connection with the present consideration is the absence of clinical manifestation of such a marked reduction in the intracranial blood supply.

Leidy (88) described a most illustrative case of thrombosis of the circle of Willis, in which there was an amelioration of symptoms until a further thrombosis caused a fatal termination; the improvement was thought to be due to the presence of an unusually large posterior communicating artery, which was found at the autopsy, and which had to some extent compensated for the obstruction. In addition to the communications at the base, the cortical branches of the cerebral and cere-

bellar arteries also anastomose, which tends to reduce the area of cortical degeneration produced by obstruction; although it is probable that the freedom of these communications is variable.

The circle of Willis has other physiological functions. It equalises the cerebral blood pressure on the two sides, and also reduces it, as seen from the investigations of Corin, who found the blood pressure in the internal carotid of the cat to equal 120 to 180 mm. of mercury, whilst in the circle of Willis it was only equal to 80 or 90 mm. As Deaver has demonstrated, the tortuosity of the vessels at the base diminishes the risk of apoplexy.

It now becomes necessary to briefly consider the individual arteries separately, stating the symptoms which would ensue from their occlusion according to the distribution described.

Vertebral Artery.

Embolism is found to be rare, but, when it occurs, is seen more frequently on the left side.

Part I. shows that an embolus would tend to be arrested at three points where there may be considerable diminution in diameter.

1. *Immediately beyond the point where it perforates the dura in fully* 50 *per cent.*—Provided the lumen remained patent distal to the site of obstruction, occlusion here would only cause interruption of the blood supply through the inferior set of bulbar branches. This would result chiefly in degeneration of a few pyramidal fibres and the caudal part of the spinal nucleus of the trigeminal nerve, both on the same side as the lesion. The clinical manifestation of the latter is difficult to decide, as many writers maintain that this part of the fifth nucleus receives pain and thermal impulses conducted by the fibres in the ophthalmic division, whilst Woods (158) is of the opinion that it receives similar impulses from a narrow strip of skin extending from the vault of the skull to the chin, just in front of the ear.

The caudal limit of the nucleus and tractus solitarius might be affected also, which would cause probably some impairment of the sense of taste in the posterior part of the tongue on the same side, and disturbance of the fibres in Gower's tract.

Campbell's (32) case of thrombosis of the inferior cerebellar artery is an ideal example of the result of occlusion of the vertebral at this level. Undoubtedly it was primarily a case of thrombosis

of the former artery, but it is clear from the history and microscopic examination that the cerebellar artery had a low origin from the vertebral and failed to provide any branches for the retro-olivary region, and that the symptoms were due to extension of the clot to the caudal part of the vertebral.

The observations in Parts I. and II. elucidate all the difficulties experienced by the reporter, and make the interpretation of the case much simpler. The careful histological examination illustrates most beautifully (although not realised by the reporter owing to deficient anatomical details) the distribution described of the inferior set of bulbar branches; paresis of the arm and leg on the side of the lesion supports the conclusion that the vertebral supplies a portion of the lateral cerebro-spinal tract at its formation.

Menzies' (97) case, in which the symptoms were also thought to be due to occlusion of the inferior cerebellar artery, is similar; only, in this instance a note is made in the report of the extension of the clot to the caudal part of the vertebral.

2. *At the normal origin of the posterior inferior cerebellar artery.*—A narrowing at this level was found four times on each side. Occlusion here would almost inevitably also result in suspension of the bulbar supply of the posterior inferior cerebellar artery, and, as it would appear impossible to make a differential diagnosis from simple occlusion of the latter vessel, its consideration will be partially deferred until that vessel is discussed.

This investigation has introduced two facts which may assist both in localising an embolus at this level and differentiating direct occlusion of the posterior inferior cerebellar from that which is secondary to obstruction of the vertebral at its origin. *If there is any paresis of limb or trunk muscles the vertebral must be affected, alone or in addition to the posterior inferior cerebellar artery. Furthermore, if there is any paresis of limb or trunk muscles without any tactile anæsthesia, with or without symptoms of a retro-olivary lesion* (i.e. *the so-called posterior inferior cerebellar syndrome*), *the vertebral is occluded probably about the mid-olivary level and not at its cephalic extremity.* The paresis in these cases would be "crossed," as the lesion must be situated above the pyramidal decussation. These important anatomical conclusions are supported by the clinical histories and also pathological examinations of cases described as occlusion of the posterior

inferior cerebellar. In Spiller's (129) first case there was some weakness of the limbs on the side opposite to the lesion, and at the autopsy the clot was found to occlude both the posterior inferior cerebellar and vertebral arteries. In Wilson's (156) case, which survived, of supposed occlusion of the posterior inferior cerebellar artery, there was some weakness of the leg on the side of the body opposite to the lesion. The cases reported by Stewart (133) and Hun (77), which have been proved at the autopsy to be uncomplicated examples of posterior inferior cerebellar occlusion, failed to show any motor paresis.

3. *At the cephalic extremity.*—Obstruction at this level would probably cause hemiplegia and hemianæsthesia on the opposite side of the body, but, what is in contradiction to the teaching of most medical treatises, need not invariably produce such symptoms. The paralysis and anæsthesia need not be necessarily so widespread, owing to the supply in this region from the anterior spinal and basilar, as the injections clearly and emphatically show that total suspension of the bulbar distribution of one vertebral need not cause inevitably complete hemiplegia. There would also be some paresis of the tongue muscles on the same side. And, owing to the fact that at this level the vertebral has, as a rule, very considerably replaced the posterior inferior cerebellar artery, the above manifestations would be associated probably with the symptom-complex described as a result of occlusion of the latter vessel.

Spiller (130) devised a symptom-complex for occlusion of the uppermost part of the anterior spinal and adjoining portion of the vertebrals, and described the symptoms of an alleged example. His case reads like a case of obstruction of the lower end of the basilar from embolus, as the onset was sudden and the symptoms were spastic paresis of all the limbs with some disturbance of the sense of position and movements of the tongue—precisely the symptoms expected after occlusion of the most caudal limit of the basilar; furthermore, simultaneous occlusion of both vertebrals appears a most unlikely occurrence.

Handford's (68) incomplete report of the symptomatology and autopsy of a case of thrombosis, in which there was gradual increasing weakness of the arm and leg on one side, dysphagia (nucleus ambiguus), and death from extension of the clot to the other vertebral and basilar, is more instructive. Duffin (52) records a very similar case. Taylor (138) describes another excellent

example of embolism of the vertebral at this level, in which there was numbness of the opposite arm and leg and the loss of the power of deglutition, which resulted in death from starvation. Wilks (153) reported five cases of what Duménil designated labio-glosso-laryngeal paralysis, and four of these appear to be probably examples of vertebral occlusion. Ormerod's (105) first case of obscure bulbar and pontine disease, together with several cases of supposed posterior inferior cerebellar occlusion, read like cases of obstruction of the vertebral at this level, with possible extension of the clot to the basilar. In 8 per cent. abducent paralysis on the same side is to be expected.

Thrombosis would cause more extensive obliteration of the lumen than embolism, and some or all of the above symptoms might be produced, but, as elsewhere, the differential diagnosis would be facilitated by the more gradual onset, with possibly remissions. Thrombosis of the vertebral is certainly more frequent than embolism.

Pope (109), in 1889, described a case of thrombosis of the vertebral associated with unilateral loss of taste at the back of the tongue, palatal paralysis, dysphagia, and paresis of the arm and leg. From the gross findings at the autopsy, he attributed the former to pressure of the plugged artery on the vagus and glosso-pharyngeal nerves, but it appears likely that our present neurological knowledge and improved histological methods would have shown that obliteration of the bulbar supply of the vessel was the true cause. The account of even such an old case illustrates the application of many of the anatomical features observed in the preceding pages.

I have searched the carefully kept records of the medical post-mortem examinations for the last twelve years at the Manchester Royal Infirmary, and have only succeeded in finding one case of occlusion of the vertebral artery in 1887 autopsies. This was on the left side and due to thrombosis, but unfortunately no clinical notes were available, as the patient was moribund on admission.

Anterior Spinal Artery.

The size and other anatomical features of this vessel suggest its immunity from embolism, and it is obvious that the very numerous reinforcements received throughout its course and the free anastomosis with the posterior spinal system tend to prevent any widespread occlusion. The rarity of its obstruction is further emphasised by the fact that I have been able to find only one authentic case reported in the literature. This was described by Coupland (35) in 1889. The symptoms were sudden

right hemiplegia without loss of consciousness, followed by paralysis of the left arm and leg, and some dysphagia; the level of the thrombosis is not described, but the softening was only seen at the pyramidal decussation. Two points are of extreme interest, and were not discussed by the reporter: first, the absence of anæsthesia, which is explained by the fact that the anterior spinal at the level of the motor decussation does not supply the fibres conveying tactile impulses; and secondly, the dysphagia, which suggests implication of the vertebral, although in one case the anterior spinal was seen to supply a branch to the postero-lateral sulcus.

The clinical importance of the investigation of origin of the anterior spinal, and the question of fusion of its two parts, may now be considered. In those cases in which the artery arises by a single stem (9 per cent. on the left, 3 per cent. on the right, and in 3 per cent. from the angle formed by the junction of the two vertebrals), the cephalic portion is much more predisposed to complete occlusion, since the anterior spinal is known to fill from above, and is more likely to be affected by occlusion of the vertebral from which it gains origin, since the possible collateral channel of the opposite side is absent. If the two branches of origin fail to fuse or communicate (6 per cent.) until they reach the cord, it is clear that the obstruction of one need not cause bilateral symptoms, although it has never been realised that anterior spinal thrombosis may cause hemiplegia and hemianæsthesia. In cases of normal distribution the clinical manifestation of symptoms will vary according to the site of the occlusion. If the obstruction was in the region of the upper part of the medulla, the symptoms would probably be paralysis of the muscles of the trunk, arms, and legs and the extrinsic and intrinsic muscles of the tongue, associated with anæsthesia of the skin except in the trigeminal region. Respiratory failure or other pulmonary or cardiac disturbances would cause, almost inevitably, a fatal termination either immediately or in a very short time. In the lower part of the medulla the clinical manifestations are perfectly illustrated by Coupland's case, with the exception of dysphagia, which would not be expected frequently. If the occlusion occurred in the spinal course it would probably be very limited, owing to the numerous reinforcements, and only cause paresis of a few muscles as a result of anæmia of the grey matter of the anterior cornua of one or more segments. Degeneration in the white matter, unless an extensive thrombosis occurred, would be largely prevented by the anastomoses with branches of the posterior spinal system.

An interesting case, the symptoms of which Ross (116) thought to be due to obstruction of several of the lumbar spinal arteries, is reported by Hamilton (67), in which paraplegia occurred after the development

of an aneurysm of the abdominal aorta, in the region of the origin of the renal arteries, although there was no possible compression of the cord. The significance of the spinal reinforcing vessels has been further illustrated by the experiments of Schiffer (120) and Weil (152), in which the aortæ of animals were ligatured, and paralyses demonstrated as a result of anæmia of the lumbar cord.

Posterior Spinal Artery.

The cause of the rarity of occlusion of this artery is similar to that described for the anterior spinal; in fact, its involvement must be usually secondary to obstruction of either the vertebral or posterior inferior cerebellar arteries. For clearness it has been considered separately, although clinically it is not recognisable, except under the conditions described in the section on occlusion of the minute nutrient branches. Its occlusion would cause impairment or absence of tactile sensibility on the same side, with probably some ataxia and giddiness owing to degeneration of some of the fibres in the dorsal and caudal part of the inferior cerebellar peduncle.

Posterior Inferior Cerebellar Artery.

As this artery is the largest branch of the vertebral and usually arises almost in the direct line of the parent trunk, it is predisposed anatomically to occlusion by emboli. For reasons previously stated, the left will have a greater tendency than the right. In 17 reported cases, the lesion was on the left side in 14, although it is necessary to state that in several of these the vertebral was found also to be plugged by clot at the autopsy. The frequency on the left is therefore marked clinically and anatomically. The described retro-olivary syndrome resulting from obliteration of the posterior inferior cerebellar artery is familiar to all neurologists, and it seems to have received attention at the expense of the other vessels, especially the vertebral.

An attempt has been made previously to show that Campbell's and Menzies's atypical cases were really clinical manifestations of occlusion of the vertebral.

Ormerod's (105) case was obviously also an example of vertebral obstruction.

The cases reported by Spiller (two), Thomas (140), and Senator (121) were found to show vertebral thrombosis at the autopsy. Wilson's (156) and Courtney's (36) cases both survived, but clinically showed indications of some slight affection of the region supplied by the vertebral.

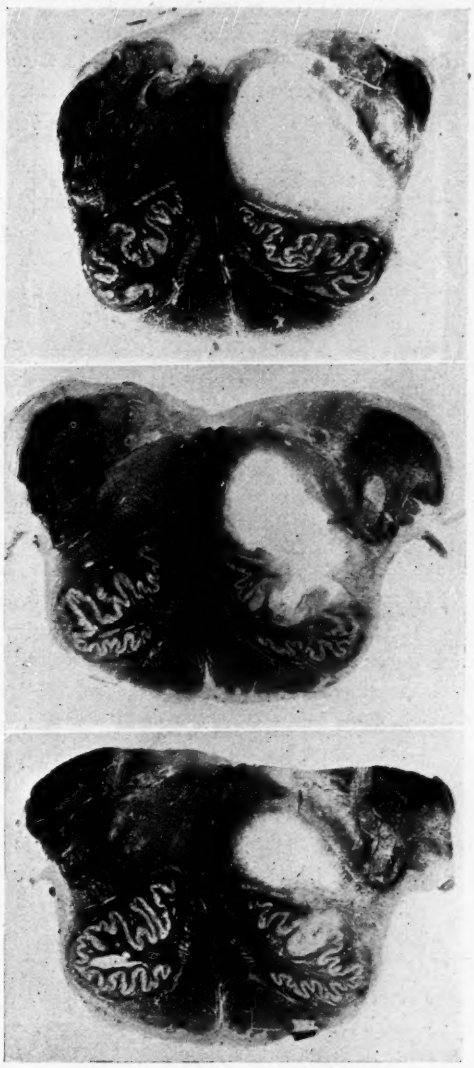

FIG. 23.—Photomicrographs from Dr R. M. Stewart's case of occlusion of posterior inferior cerebellar artery.

Stewart's (133) and Hun's (77) cases were proved to be true uncomplicated cases of posterior inferior cerebellar thrombosis. The clinical histories of the cases reported by Abrahamson (1), Gillis (case 2), Judson Bury and the writer (30), Head and Gordon Holmes (71), Harris (69), and Robinson (113) suggest no involvement of the vertebral, but without an autopsy it is impossible to exclude this possibility. This rapid survey of 17 cases reported as occlusion of the posterior inferior cerebellar artery shows the confusion with the vertebral, and the difficulty of excluding extension of the clot to the latter vessel. The anatomical study of the distribution of these two arteries unfortunately has failed to assist directly—in fact, it has shown that occlusion of either vessel may cause precisely the same symptoms; but the following conclusions may indirectly help in some instances, and prevent all cases exhibiting the retro-olivary syndrome being unreservedly reported as examples of thrombosis of the posterior inferior cerebellar artery.

1. Any paresis of trunk or limb muscles definitely denotes vertebral or anterior spinal involvement.

2. The vertebral may nevertheless be occluded without any manifestation of paresis of the trunk or limb muscles.

3. The vertebral may absolutely replace the bulbar supply of the posterior inferior cerebellar. In a few of these cases its complete occlusion would cause symptoms which are identical with the syndrome described for the latter vessel, without any additional clinical manifestations which would indicate the artery affected.

4. Crossed hemianæsthesia to pain and thermal stimuli unassociated with dysphagia and laryngeal paralysis is most probably due to vertebral occlusion, as the spino-thalamic tract is never supplied by the posterior inferior cerebellar artery below the lowest limit of the nucleus ambiguus.

Gillis's (62) first case has not been included in the previous 17, and merits special reference.

Briefly, the symptoms were analgesia and thermal-anæsthesia over the area of skin supplied by the ophthalmic and superior maxillary divisions of the trigeminal nerve on the right side and the whole of the left side of the body below the nipple. There was no paresis of the pharyngeal or laryngeal muscles, but the usual sympathetic disturbances were present, as well as a more marked patellar reflex on the right side. The history suggests obstruction of the lowermost bulbar branches of the vertebral, as in Campbell's and Menzies's cases, but in the latter there was the extra

assistance in diagnosis obtained from the post-mortem examination. The unusual distribution of the analgesia is very significant, although neglected by the reporter of this case. Its absence in the region supplied by the second, third, and fourth cervical nerves suggests that their fibres conveying "pain" and "temperature" impulses had not crossed at the level of the lesion, which was therefore probably lower than the region supplied by the posterior inferior cerebellar artery. This supposition, together with the absence of any signs of involvement of the nucleus ambiguus, coincides with the opinion that the case is really an example of vertebral occlusion about the level of the pyramidal decussation. This suggestion with regard to the level of crossing of pain and thermal fibres of the upper cervical nerves requires further investigation, but I offer it provisionally as a new and most useful guide to localisation.

Most of the recorders of cases maintain that the symptoms of posterior inferior cerebellar occlusion are extremely constant. Neither careful study of the reported examples nor the anatomical distribution supports this, and greater care ought to be adopted in the selection of examples of this interesting type of bulbar palsy. I do not intend to enumerate the symptoms, as they have been described repeatedly, and my intention is more to indicate the difficulty in excluding other vessels whose occlusion may cause identical symptoms.

Dr R. M. Stewart, medical officer at Prestwich County Asylum, has very generously supplied me with the carefully prepared sections of the medulla from his proved case of posterior inferior cerebellar occlusion. Photo-micrographs, at the most instructive levels, are seen in fig. 23, and they will be seen to strikingly resemble the area of distribution ascertained by injection.

Basilar Artery.

For the anatomical reasons stated, embolism of this artery is very rare, and practically only seen at its bifurcation to form the two posterior cerebral arteries. Chadwick (33) and Maudsley (96) each report one case of embolism of the basilar at this point.

Occlusion of this vessel, from embolism or thrombosis, must almost inevitably result in death, as it will cause degeneration of all the descending fibres on both sides, including those which pass to the vital centres in the bulb and caudal part of the pons. The rapid death in these cases from asphyxia was recorded in 1868 by Hayem (70), and extension of the thrombus to the basilar has been seen to herald a fatal issue in several cases of vertebral occlusion.

Bastian's (11) case may be cited as a typical illustration of basilar

obstruction, in which there was an apoplectic seizure followed by profound coma, irregular stertorous breathing, absence of reflexes, and death in five and a half hours. In some cases there is conjugate deviation of the eyes and rotation of the head, as described by Eichhorst (57). Many have recorded hyperpyrexia.

Weber (150) gave an account of a case of thrombosis of the basilar of unusual etiology, the clot being secondary to a gumma which arose from the lining of the cephalic extremity of the right vertebral.

Thomson (141) described a valuable case of supposed pontine thrombosis. There was anæsthesia to all forms of stimuli over the left side of the face, partial thermal anæsthesia of the left leg and left side of the trunk, but in the latter situation there was also some analgesia and impairment of the tactile sensibility. Sensory disturbances of the skin of the left arm were "barely noticeable."

In addition, there was loss of taste on the left side, and the left leg was ataxic. The onset was sudden, and undoubtedly indicated vascular origin, but I suggest that it cannot be due to any pontine obstruction, chiefly because the fibres from the gustatory epithelium pass to the nucleus solitarius, which is not found in the pons. The associated affection of the nucleus (or tractus) solitarius, spino-thalamic tract, and some of the medial lemniscus fibres (as obviously the tactile fibres must have crossed, since they are impaired on the same side as the "pain" and "temperature" fibres which cross in the cord) without any involvement of somatic or splanchnic efferent fibres suggests a lesion between the lowest limit of nucleus ambiguus (about the level of the sensory decussation) and the formation of the lateral cerebro-spinal tract. Reference to the discussion of posterior inferior cerebellar and vertebral occlusion will make this clearer. A lesion at this point, if of vascular origin and not due to hæmorrhage, could only be caused by obliteration of the inferior bulbar branches of the vertebral. In fact, very slight variation in the normal distribution of this vessel might cause it; the fifth nucleus might easily escape and a few fibres of the medial lemniscus be included. The sole objection to this theory is the very complete anæsthesia in the trigeminal area, but lack of accurate information prevents this being definitely dealt with, and it is not so insurmountable as the contra-indications to the localisation in the pons.

As complete occlusion of the basilar is almost invariably fatal and must cause most extensive symptoms, no advantage can be gained by enumerating the results of such a calamity. Ross (116) has referred to the possibility of attachment of a thrombus to the wall of the vessel causing merely obliteration of a few branches. If this occurred in the upper

part of the pons the result would be paralysis of the fourth and possibly also the third cranial nerves on the same side, with complete paralysis of the muscles of limbs, trunk, mastication, face, palate, tongue, and pharynx, and hemianæsthesia (to all types of sensation) on the side opposite to the lesion. In the lower part the sixth nerve and muscles of the face and mastication would be paralysed on the same side, and the muscles of the limbs, trunk, palate, tongue, and pharynx on the opposite side. Owing to our imperfect knowledge of the arrangement of the trigeminal fibres it is impossible to state accurately the distribution of anæsthesia of the face, but the limbs and trunk would be anæsthetic (to all types of sensation) on the side opposite to the obstruction. It is necessary to repeat that in 19 per cent., owing to the more caudal origin, the basilar supplied the upper part of both hypoglossal nuclei, and in 9 per cent. the vertebral, as a result of the more cephalic origin of the basilar, supplied the abducent nucleus.

The Anterior Inferior and Superior Cerebellar Arteries.

Owing to their origin being almost at right angles to the basilar, these vessels are rarely obstructed by embolism. Their distribution to the pons is too indefinite to justify the description of any symptomatology in connection with their occlusion, except to say that affection of the anterior inferior cerebellar artery would probably result in some disturbance of the auditory and vestibular fibres.

(B) *Occlusion of the small Bulbar or Pontine Branches.*

These small end arteries may be occluded by a thrombus, minute embolus, or even by an obliterative arteritis. Nervous diseases of syphilitic origin probably provide the most interesting examples of the latter cause.

The much-discussed vascular etiology of innumerable diseases of the central nervous system has been previously mentioned, but its final decision must be left to the clinician and the pathologist, and the necessity to them of accurate anatomical data is obvious.

Recently several obscure cases of bulbar and pontine degeneration have been described, and, in the absence of more definite explanations, sclerotic changes in the nutrient blood-vessels have been alleged as the cause. The varying range of nervous symptoms and pathological discoveries in cases of arterio-sclerosis, combined with inadequate accounts of the distribution of the bulbar arteries, are the probable reasons for this supposition.

Space only permits reference to two cases which may be cited as examples.

Spiller (128) reported a case suffering from complete bilateral oculomotor paralysis, rigidity of the limbs, and stertorous breathing. The onset was sudden, and the suggested cause was thrombosis of the small blood-vessels supplying the nuclei of the third nerve on each side, which at autopsy exhibited softening. Unfortunately, the notes are far from complete, but a more acceptable diagnosis of this case appears to be embolism of the basilar at the point where it bifurcates to form the posterior cerebrals. This would be a simpler and equally efficient explanation of the condition, and would be in absolute agreement with the anatomical researches described in this thesis and by other observers. It is difficult, from the symptoms described, to imagine why this diagnosis was ignored.

The other selected example of obscure paralysis alleged to be possibly due to sclerotic changes in the nutrient blood-vessels has just been described by Taylor (137). The disease is hereditary, occurs after the fiftieth year, and terminates fatally. The only symptoms are bilateral ptosis and dysphagia. The ocular movements and phonation are normal. Precisely the same clinical manifestations have been noticed in two generations of the same family. The constancy of the symptoms and the association of such anomalous palsies point against a vascular etiology, and the study of the distribution of individual groups of the minute bulbar and pontine branches makes such a supposition untenable.

It is quite beyond the range of possibility to imagine such a coincidence as the bilateral occlusion of the small vessels supplying the cells giving origin to the fibres innervating the levator palpebræ superioris muscle in members of two generations, even if the curious association of dysphagia was eliminated. The suggestion that the symptoms are due to obstruction of the larger vessels is no more justifiable, and it would appear wiser not to hazard any explanation rather than cloak our ignorance with such an impossible and unscientific one. Most of the suggested examples of occlusion of minute bulbar or pontine branches appear equally unjustifiable, when studied in conjunction with the anatomical distribution of the arteries.

Conclusions to Sections A and B.

The conclusions conveyed by the review of the more important reported examples of vascular lesions of the bulb and pons coincide with the opinions and observations expressed in the purely anatomical parts, and intensify the immense difficulties to contend with in attempting to diagnose and localise cases of arterial occlusion. The demand for still further research in the arrangement and function of the nuclei and tracts enumerated in the preceding pages is very apparent. The danger and

inevitable failure resulting from a too stringent regard for the various syndromes is manifest.

Practically all the vessels are subject to such wide variation in distribution that it is quite inadvisable to associate emphatically a single group of symptoms with any one artery. A good illustration of the result of placing too much reliance on a syndrome is seen in the case of the posterior inferior cerebellar artery, where it seems to have caused many inaccurate diagnoses, and probably sometimes prevented efficient examinations being made, owing to the ease with which this freely published group of symptoms may be applied to occlusion of other arteries.

The most important conclusion, then, appears to be that every case must be most diligently examined and judged on its own merits, regardless of any syndrome, if the affected vessel and the position of the obstruction are to be accurately defined. Vague unsupported diagnoses are to be deplored, as they must tend to depreciate rather than advance our knowledge.

It seems possible that more careful clinical records, extensive pathological examinations, and further anatomical research may overcome many of the difficulties described.

II. The Significance of the Neuro-Vascular Relationships.

All the cranial nerves, with the exception of the olfactory, have a longer or shorter intracranial course before they emerge from the skull. During the greater part of that course they lie in intimate relation with the bones of the cranium, and in consequence are very susceptible to compression. The exciting causes of compression are numerous, but it is only intended to refer here to those of vascular origin. The conditions of an artery, under which it is possible for a nerve to be compressed against a resistant structure like bone, may be grouped into three classes:—

1. Arterio-sclerosis, or any degenerative or inflammatory condition by which the arterial wall is thickened and rendered harder and less elastic.
2. Aneurysm. Usually only the slow-growing, thick-walled type or those exhibiting calcification manifest compression symptoms. Beadles (14) found a history indicating compression of one or more cranial nerves in 14 per cent. of the cases of aneurysm of the larger cerebral arteries.
3. Possibly vascular spasm may result in serious pressure upon cranial nerves. This cause is naturally obscure and its existence difficult to prove, but it is nevertheless necessary to mention it.

Illustrative cases of the first two, and possibly the latter, causes of palsy of the cranial nerves are to be seen in the literature, and a few will be mentioned subsequently. Whilst reading the reports of these cases it is evident that the writers have experienced great anatomical difficulties owing to the omission of neuro-vascular relationships, a clear knowledge of which is required by many of the writers.

The possible compression of cerebral nerves by arteries has been realised for some considerable time, but more recently writers have directed our attention to the possible "constriction" of nerves by vessels. Cushing (40) has very clearly marshalled the facts of this important subject before us and brought strong evidence to support the view that, in conditions which cause enlargement of the brain stem, the arteries which extend laterally tend to be stretched, and consequently constrict the nerves if the former are situated ventral to the latter. He examined very carefully 39 cases of intracranial tumour and found "grooving" of the pons by normal (not sclerosed) transverse arterial rami in 21, and in 10 of these the growth was subtentorial. This grooving was seen only once in a control series of 20. He further showed evidence of a similar constriction of certain cranial nerves, especially the third and the sixth. In 11 cases out of 14 which displayed symptoms of ocular disturbance during life, he found evidence of arterial constriction at autopsy. In this paper Cushing regrets the lack of anatomical information about the normal relations between these nerves and arteries within the cranium; and, even if his conclusions will not account for the nerve palsies in so many varying lesions as he suggests, it is necessary to extend our present knowledge of the normal state in order to better understand and interpret morbid conditions.

Each nerve will be briefly considered separately, as this appears more practicable than a separate study of the vessels:—

1. *Olfactory nerve and tract.*—No artery of any size is related to the minute branches of this nerve as they pass through the cribriform plate, but the tract may be affected by large aneurysms of the basal trunks. Beadles (14) mentions an instance of aneurysm of the intracranial portion of the internal carotid which seriously damaged the left olfactory tract.

2. *Optic nerve, chiasma, and tract.*—The intimate relation between the terminal part of the internal carotid and the optic nerve, chiasma, and tract is well known. In any of these three parts of their course the optic fibres may be compressed by pathological conditions of the internal carotid.

Many cases have been reported of damage being done to these fibres by

aneurysm, but it is not realised that simple atheroma of the internal carotid may mechanically produce optic atrophy, as the nerve is not placed in such a favourable position for compression as many of the others. Elliot Smith (123) has reported one case and seen five others where this has occurred. This factor in the production of optic atrophy is persistently disregarded by ophthalmologists, although, since there is repeated evidence in the dissecting-room of pressure on the optic nerve being exerted by a diseased internal carotid artery, it appears evident that the clinical and pathological aspects of this subject require investigation.

On the other hand, the compression of the optic nerve by the ophthalmic artery against the optic foramen has received attention, and cases have been reported by Bernheimer (23).

It is quite clear that the optic chiasma may be compressed against the cranial base by an aneurysm of the anterior communicating artery. Mitchell's (98) case, in which bitemporal hemianopsia was produced by the pressure of an aneurysm of an anomalous communication between the two internal carotid arteries, has previously been noted. The only other example of bitemporal hemianopsia due to aneurysm was reported by Bramwell (27), and on this occasion the internal carotid was the affected vessel.

3. *Oculo-motor nerve.*—Aneurysm of the internal carotid has frequently caused paralysis of the third nerve; the position of the two in the cavernous sinus fully explains this, and the associated involvement of the fourth, sixth, and ophthalmic division of the trigeminal makes the localisation of the lesion usually a simple task.

Delpech (46) recorded a case of compression by an aneurysm of the cephalic part of the basilar.

Beadles (14), in his collection of 555 cases of aneurysm of the larger cerebral arteries, found that the oculo-motor was the nerve most frequently compressed by aneurysms of the posterior communicating artery, and that dilatation of this vessel clinically produced mechanical symptoms more frequently than any other (47 per cent.).

Aneurysm of the posterior cerebral or superior cerebellar arteries, near their origin from the basilar, must also easily cause oculo-motor palsy. This nerve lies in the angle formed by these two vessels at their origin, but the intimacy of this neuro-vascular relation is subject to some variation. In the majority, the two arteries arise practically by a common trunk, and consequently atheroma

of either may easily produce ocular disturbance. Owing to the constant anatomical disposition of the posterior cerebral, which extends transversely cephalic to the nerve, it is possible, as Cushing has shown, for the artery to indent the third nerve in cases of cerebral tumour accompanied by any considerable alteration in the position of the brain stem.

Therefore oculo-motor palsy may result from aneursym of the internal carotid, basilar, posterior cerebral, and superior cerebellar arteries, or atheroma of the two latter, or even constriction by a normal posterior cerebral under certain pathological conditions.

The third and more disputed type of palsy due to vascular compression may be illustrated by this nerve. Many writers have published accounts of recurrent oculo-motor paralysis. The affection may be limited to one division of the nerve or even a single muscle, and no decisive pathology is known. It has been repeatedly suggested that the attacks are due to vascular spasm or paralysis of the vaso-motor nerves causing distension of the vessels and consequent compression of the nerve.

Fleming (60) has recently described an example of this condition in a girl of twelve, in which there were three attacks in three years. The disease is often associated with migraine, which is rather significant, as two theories for its etiology lend support to the suggested cause of transient and periodic oculo-motor paralysis. Some maintain that migraine is of vascular origin, whilst Spicer, Holmes, and Ormerod (127) consider it as secondary to cerebral œdema, a condition which could disturb the position of the brain stem, and consequently produce constriction of the third nerve, and similarly the sixth, paralysis of which is sometimes associated in these cases.

4. *Trochlear nerve.*—Special consideration of this nerve is unnecessary, as its position obviously renders it liable to compression by aneurysm of the same vessels as the third.

5. *Trigeminal nerve.*—The ophthalmic division may clearly be affected by aneurysm of the internal carotid in the cavernous sinus, but it is not so apparent that the other divisions may be affected through compression of the gasserian ganglion by the same vessel. Hutchinson (75) has recorded an excellent example associated with paralysis of the external rectus.

Romberg (114) described a case of intermittent neuralgia due to irritation of the gasserian ganglion by a rigid dilated internal

carotid artery. Basilar aneurysm, especially the saccular type, may exert pressure on this nerve proximal to the ganglion.

6. *Abducent nerve.*—Reference has previously been made to affection of this nerve during its passage through the cavernous sinus, and many examples are to be found in the literature. But its possible compression against the basi-sphenoid appears to have been completely neglected. My examinations (see fig. 24) have shown that the nerve is in relation to this bone for fully half an inch, as it passes from its superficial origin to the cavernous sinus, and that the anterior inferior cerebellar artery is dorsal to the nerve (*i.e.* may compress the nerve against the bone under certain conditions) in 14 per cent. on the right side and

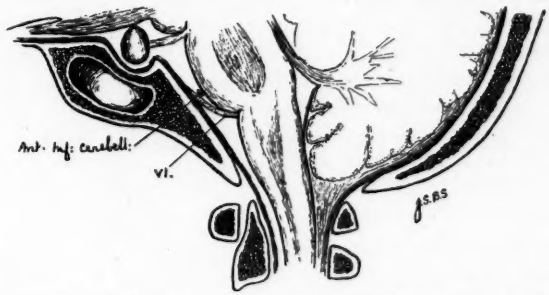

FIG. 24.—To show possible compression of sixth nerve by anterior inferior cerebellar artery.

19 per cent. on the left. It is easy to see that an atheromatous vessel in this percentage might easily produce convergent strabismus, and very deep "grooving" of the nerve from that cause has been seen once in this investigation; and it is important to note that in this case the artery was in the ventral position, and had no resistant structure to compress the artery against. Space does not permit further discussion of this point, but it offers a feasible explanation of uncomplicated sixth-nerve paralysis, which has been unscientifically attributed to "its long course and exposed position."

Some years ago I saw a case which now appears to be probably an illustration, as the patient suffered from chronic nephritis and arterio-sclerosis in addition to the transient paralysis of the external rectus of one side, which at the time of examination defied explanation. There was no suspicion of syphilis, and

the man recovered from the paralysis in a few weeks and is alive to-day, but unfortunately I have been unable to hear whether the paralysis has ever recurred.

Strangulation or constriction of the abducent can only occur when the artery occupies the ventral position; and from Cushing's results, this certainly appears to account for the frequent occurrence of affection of this nerve in cases of cerebral tumour, and possibly in several more obscure nervous diseases owing to the associated cerebral œdema.

7. *Facial and auditory nerves.*—These two nerves pursue the same course from their superficial origin to the internal auditory meatus, and for the greater part of this course are in contact with the petrous portion of the temporal bone. Consequently any compression paralysis of one is likely to be accompanied by paralysis of the other, and associated with loss of taste on that side owing to affection of the pars intermedia.

Loomis (91) has given an account of a case of saccular aneurysm of the basilar, which suffered from deafness, facial paresis, and loss of taste on the affected side, as well as symptoms resulting from compression of the trigeminal and hypoglossal nerves and the pyramidal fibres.

Hale White (66) has described a case of aneurysm of the vertebral which resulted in facial paralysis.

From the examination of a number of examples of advanced arteriosclerosis of the vertebral it seemed likely that this condition might easily cause compression of the seventh and eighth nerves, as the elongated sclerosed vessel was very frequently displaced laterally and found in contact with these nerves in the cerebello-pontine angle.

In Part I. it has been stated that the anterior inferior cerebellar artery usually crossed these nerves dorsally, and therefore it is easy to see how diseased conditions of this vessel might compress them against the bone. In the few where the artery crossed ventrally, the nerves would be in danger of constriction under the conditions mentioned by Cushing with regard to the third and sixth nerves. Ogle (104) reported an example of "stretching" of the facial nerve by aneurysm of the anterior inferior cerebellar artery.

8. *Glossopharyngeal, vagus, accessory, and hypoglossal nerves.*—All these nerves lie in contact with the occipital bone before they emerge from the cranium.

Compression by aneurysm of the vertebral is obviously possible, and several instances have been recorded. The hypoglossal has been most frequently affected, as is to be expected from the intimate relation which normally exists between the artery and this nerve. Aneurysm of the lower part of the basilar will also endanger the same nerves, and Klippel and Boetean (84) described such a case in which the patient suffered from persistent dysphagia, pharyngeal anæsthesia, palatal paresis, and defective speech.

Lebert (87) and Kingston (83) have each recorded instances of paralysis of the vagus and hypoglossal nerves associated with symptoms indicating compression of the pyramidal fibres as a result of aneurysm of the caudal part of the basilar.

From the position of the vertebral artery discovered in cases of advanced arterio-sclerosis it appeared reasonable to suppose that this condition might produce paralysis of one or more of the above nerves by compression, although no standard medical work is prepared to admit it. It appears infinitely more probable than compression of the optic nerve by an atheromatous internal carotid, proved illustrations of which have previously been quoted.

9. "*Grooving*" *of the brain.*—In conclusion, it is necessary to refer to the possible mechanical effect of the foregoing pathological conditions of the vessels upon the brain itself.

On several occasions aneurysm of the basilar or vertebral have compressed either the pons or medulla sufficiently to produce a depression, and this has resulted in clinical symptoms in several of the cases quoted. From their anatomical position the pyramidal fibres, either in the pons or medulla, are most exposed to such compression, and I have been unable to find reports of the clinical manifestation of compression of any other part of the brain tissue. Similarly, arterio-sclerosis may cause compression symptoms, and deep transverse grooving of the medulla has frequently been seen in the dissecting-room when marked sclerosis of the vertebral artery has existed.

Cushing found grooving of the pons, produced by *normal* transverse branches of the basilar, 25 times in 39 cases of cerebral tumour; therefore it is only likely that a sclerosed artery may cause considerable disturbance.

The compression of the brain or cranial nerves by aneurysm is generally realised by all, but the *conclusion* to be drawn from the examination of a series of diseased vessels is that it appears probable that simple arterio-

sclerosis may mechanically produce symptoms more frequently than text-books suggest, and that many obscure palsies of the cranial nerves (especially the sixth) may in the future be proved to be a result of this condition.

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FURTHER STUDIES ON THE PERITONEUM AND INTESTINAL TRACT IN MONOTREMES AND MARSUPIALS.

By W. Colin Mackenzie, M.D. (*From the Laboratories of the Royal College of Surgeons of England.*)

In a previous communication[1] I drew attention to the presence of three primary peritoneal folds in Monotremes and Marsupials, which are traced in varying degrees throughout the Mammalia and play an important part in the fixation of the gut coadjusted to the erect posture of man:—

(*a*) Mesial fold approximating the colon to the pyloric region (see fig. 1).
(*b*) Duodenal or right lateral, passing from the ascending duodenum to the right aspect of the mesocolon (dorsal mesentery) of the distal colon (see fig. 1).
(*c*) Left lateral or lieno-mesocolic from the left, dorsal, or posterior process of the spleen to the left aspect of the mesocolon of the distal colon (see fig. 2).

In connection with studies on the spleen the importance was shown of the last fold as a factor in fixation of the colon in the left hypochondrium, to which dorsal fixation of the "descending" colon is subsequent. In this paper I propose to deal with the mesial and duodenal folds in the same two orders, viz. Monotremata and Marsupialia.

1. Mesial Fold.—My attention was first directed to this band in a study of the peritoneum of the koala (*Phascolarctos cinereus*). The intestinal tract of this Marsupial is characterised by the great development of the colon, which is suspended to the pyloric and commencing duodenal region by a tough fibrous band—mesial fold—measuring 1·5 cm. long and 1 cm. broad (see fig. 1). By means of this band we distinguish a left, narrow, looped distal colon and a shorter, but wider, right or proximal colon.[2]

(*a*) *Left or Distal Colon.*—This may measure 210 cm. in length. It is swung freely on its own mesocolon, the width of which may measure

[1] *Journal of Anatomy*, vol. li. part i.

[2] "Factors concerned in causing Rotation of the Intestine in Man," J. E. Frazer and R. H. Robbins (*Jour. Anat. and Phys.*, 1915, L. 75–110). In this important paper the first reference is made to a retention band in the human embryo at the "colic angle," *i.e.* junction of mid and hind gut.

20 cm., and is attached along the dorsal abdominal wall mesial to the kidneys and psoas minor muscles.

(*b*) *Right or Proximal Colon.*—This measures in an adult 150 cm., and is swung, together with the small intestine and cæcum, on the common mesentery. Thus the intestine from the duodeno-intestinal flexure to the mesial fold may be lifted in one piece; and although three divisions of the common mesentery are recognised, yet these have a single root of origin. The

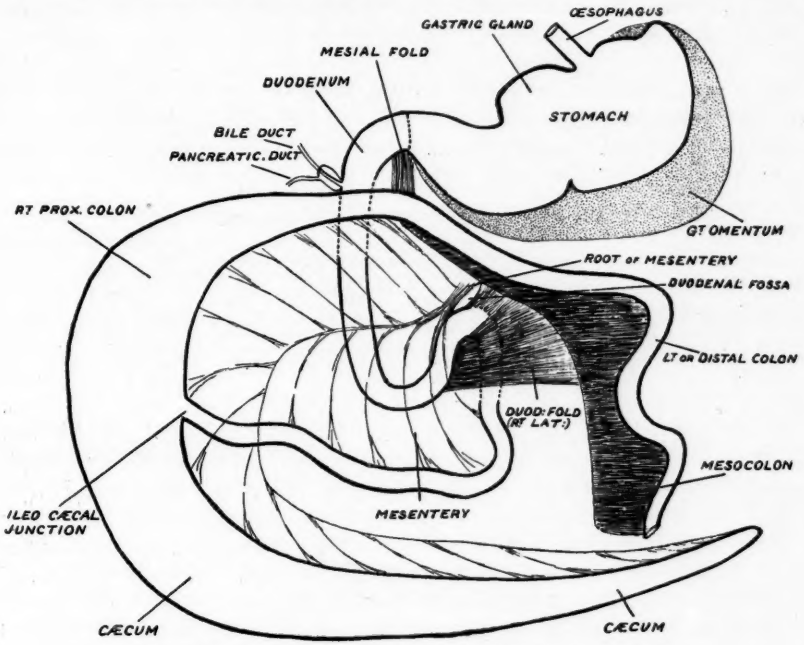

FIG. 1.—The gastro-intestinal tract of Koala (*Phascolarctos cinereus*).

greatest circumference of the right colon in the usual post-mortem state may equal that of the cæcum, viz. 15 cm.; but as we approach the pylorus it narrows, the gut becoming more contracted and the circumference 5–7 cm. The right colon is continuous with a large cæcum which represents the greatest instance of cæcal development in the Mammalia. It may reach 240 cm. in length. It tapers gradually to the blind termination, or terminates somewhat abruptly so as to give a vermiform character to the extremity, as first pointed out by Huntington.[1]

[1] *Anat. of Human Peritoneum and Abdominal Cavity*, Philadelphia, 1903.

2. Right Lateral or Duodenal Fold.—This fold I also found to be well developed in koala. The duodenum forms a somewhat V-shaped loop, and we can distinguish a descending or proximal limb 7–14 cm. long, and an ascending or distal limb 4–8 cm. The duodenal loop is swung on a somewhat narrow mesoduodenum which is free, and, together with the duodenum, can be raised off liver, kidney, and dorsal wall. The descending limb is crossed below by the root of the mesentery and above by the right colon (fig. 1). Passing from the dorsum of the ascending duodenum to the right aspect of the mesocolon of the distal or left colon, close to its dorsal attachment, is a well-defined fold which is free below. Between the upper part of the fold, the root of the mesentery on the right, and the duodeno-intestinal flexure below is a fossa—the primary duodenal fossa—which in an adult measures ·5 cm. across and 1·25 cm. long, with a depth of ·75 cm.[1]

The Folds in the Monotremes.

(*a*) *Platypus* (*Ornithorhynchus anatinus*).—From the pyloric knob the duodenum passes nearly vertically down, with a slight inclination to the right, for a distance of about 2·5 cm. to where the common duct enters (fig. 2). It then curves out for 6 cm., passing nearly horizontally to the right. After descending for about 5 cm., it finally passes in and upwards to the left, ventral to the lower pole of the right kidney, for about 5 cm., reaching the mesial line at the duodeno-intestinal flexure. In this last portion a transverse and ascending portions may be distinguished, although the latter may or may not be well developed. Thus we have a well-defined duodenal loop which is swung on a mesoduodenum or duodenal mesentery with a greatest width of 5 cm. The duodenal loop and mesoduodenum can be raised off the right kidney and dorsal wall. The distal 3 cm. of duodenum (asc. duodenum) is connected to the mesocolon of the left or distal colon by a fold—the right lateral or duodenal. This is free below; and between its upper extremity, which is usually well defined, the root of the mesentery on the right, and the duodeno-intestinal flexure below, a pocket is found. This is the primary duodenal fossa. It measures 1–2 cm. long and ·75 cm. in width.

From the duodeno-intestinal flexure we have swung on the common mesentery a portion of intestine together with the tubular cæcum (fig. 2). The part proximal to the cæcum is small gut, that distal is proximal or right colon. This right colon is 17 cm. long, and crosses the transverse

[1] "The Intestinal Tract of Mammals," P. Chalmers Mitchell, *P.Z.S.* (Lond.), 1916, i. 183–251. In this paper Dr Mitchell's more recent researches in connexion with the differentiation of gut patterns throughout Mammalia are dealt with.

duodenum, being traced upwards and to the left, ventral to the mesoduodenum, for about 6 cm. For the first 2·5 cm. of this portion, both colon and mesentery are free from mesoduodenum, though in one case I have seen bands of adhesion between colon and duodenum. We then find for the next 1·5 cm. that the mesentery is bound down to the

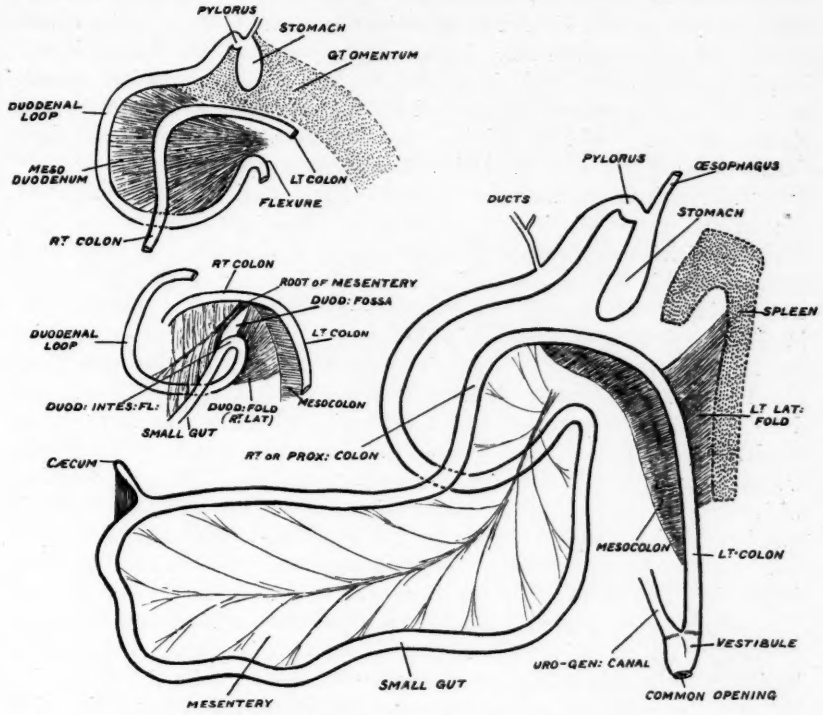

FIG. 2.—The gastro-intestinal tract of Platypus.

mesoduodenum. Then on to its termination the right colon and mesentery are adherent to the mesoduodenum, constituting a definite "fixed" part of the colon tract. The termination corresponds to the junction of common mesentery and mesocolon of the left colon, and a distinct "tucking-in" effect is noted. The distance between the "fixed" colon and duodenum is 2 cm., and traces of a band—mesial band—may be present between the two, ventral to the mesoduodenum. From the "fixed" point the left or distal colon is continued on to the vestibule. It measures 22 cm., and

is swung freely on its own dorsal mesentery or mesocolon, which is traced back to the dorsal wall between the psoas muscles and has a greatest width of 5 cm. Related to its dextral aspect is the right lateral or duodenal fold, and on its left the left lateral or lieno-mesocolic fold (fig. 2).

(*b*) *Echidna* (*Echidna aculeata*).—There is a well-defined duodenal loop, not so constant in character as in Platypus. Owing to the dorsal fixation of the pancreas there is less mobility of the loop, though it can be raised off the liver and right kidney. The first or ascending portion, 2·5–5 cm. long, passes from the pylorus to the visceral surfaces of the right cystic and right lateral lobes of the liver. The duodenum then descends for 3 cm., and finally inclines inwards and to the left for 1 to 1·5 cm.—terminal or transverse portion—dorsal to the commencement of the mesentery and proximal colon, terminating at the duodeno-intestinal flexure, which is fixed dorsally about the root of the mesentery and pancreas. Compared with Platypus there is little more than a "tucking in" of the termination of the descending duodenum—reminding one of the condition in the American opossum. A membranous band may be traced from the flexure to the mesocolon of the distal colon, and a small duodenal fossa noted; but the particular point to be noted is, that associated with the dorsal fixation of pancreas and duodeno-intestinal flexure there is no duodenal fold nor fossa in the Echidna. As in Platypus, from the flexure we have swung on the common mesentery a portion of intestine together with the appendix. The portion proximal to the appendicular region is small gut, and that distal is right or proximal colon. This measures 30–35 cm. long, and passes with the mesentery ventral to the lower part of the descending duodenum, off which it can be lifted. It then becomes fixed dorsally about the root of the mesentery, pancreas, and duodeno-intestinal flexure for about 1·5 to 3 cm. No mesial fold is present, but fixation begins opposite the pylorus. This "fixed" colon marks the distinction between the proximal and distal colon, and corresponds to the junction of common mesentery and mesocolon of distal colon. The left or distal colon is mobile, being swung on its own dorsal mesentery or mesocolon. The degree of mobility is extremely variable, however. In one specimen in which this colon was bound dorsally the total length from "fixed" point to vestibule was only 13 cm., while in another with the left colon freely mobile on a defined mesocolon the length was 28 cm.

The Folds in Marsupials.

(*a*) *Wombat* (*Phascolomys*).—There is a well-defined duodenal loop, and, as in the human, four portions may be recognised (fig. 3). It first

passes down and out for 2–3 cm., then descends for 9–12 cm., then inwards for 1·5 cm., and finally passes up and to the left of the mid line to the duodeno-intestinal flexure for 3 cm. Owing to the dorsal fixation of the pancreas, which fills the loop, the duodenum presents little independent mobility, being less mobile than in other Marsupials—*i.e.* it has a shorter mesoduodenum, although I have not met any case of actual adhesion of the descending duodenum to liver or kidney as in

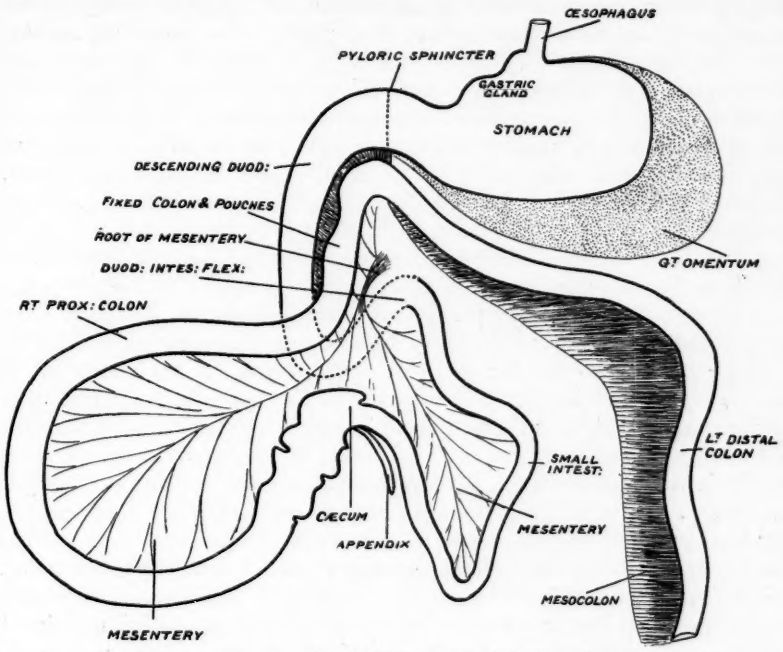

FIG. 3.—The gastro-intestinal tract of Wombat (Phascolomys).

Echidna. In relation with the distal portion there is a right lateral or duodenal fold connecting it to the dorsal wall ventral to the left psoas minor and proximal to the attachment of the mesocolon of the left colon. The fold is transverse above, being ·5–1 cm. in width, while below the lower free margin is 2–2·5 cm. in width and more oblique. Between the upper part of fold—the root of mesentery—and duodeno-intestinal flexure a small pocket is noted—primary duodenal fossa. In one specimen with the duodenum more fixed dorsally no duodenal fold nor fossa could be demonstrated, thus resembling Echidna.

The ileo-cæcal region lies close to the root of the mesentery, and may be regarded as a fixed part of intestine. The distance between this region and the attached colon at pylorus is 6 cm. The proximal or right colon extends from the ileo-cæcal junction to the pyloric region, where it is firmly attached (mesial fold). It measures 175–220 cm., and is freely mobile, being suspended like the small gut on the common mesentery. Towards its termination the right colon ascends ventral to the loop of the duodenum, pancreas, and mesoduodenum, and becomes closely applied by adhesion to the descending and first part of the duodenum as well as to the pyloric region. It is interesting to note the presence of a dilatation, or often two large pouches on the colon at the duodenal attachment. The left or distal colon extends from the pylorus to the pelvis. It measures 230–280 cm., and is swung freely on its own mesentery or mesocolon, the greatest width of which may equal 25 cm. Dorsally the mesocolon extends mesial to the two kidneys, and its length is about 15 cm.

(*b*) *Kangaroos and Wallabies* (*Macropodidæ*).—The duodenum forms a V-shaped loop ventral to the right psoas, kidney, and the liver, so that a descending and an ascending portion may be recognised (fig. 4). Either the ascending or descending limbs may be the longer, though occasionally in the wallaby the two stems may be of equal length. In the kangaroo the descending limb varies from 5–8 cm. and the ascending from 7–9 cm. The duodenum does not cross the mid line. The loop is free, and being provided with a mesoduodenum it can be raised from the psoas and kidney. Ventral to the lower part of the loop is the proximal colon and the root of the mesentery. There is a well-defined duodenal or right lateral fold connecting the ascending duodenum and the mesocolon (dorsal mesentery) of the left or distal colon. It is narrow above but wider and more oblique below, where its width may reach 3 cm., and it may be traced caudally almost to the pelvis. The finger can be passed behind the caudal margin of the fold. Between the duodeno-intestinal flexure, root of the mesentery, and the upper margin of the fold is a small but well-defined duodenal fossa. The macropod has a well-defined cæcum much larger in the kangaroo (25–35 cm.) than in the wallaby (7–12 cm.). Variability is a characteristic of the wallaby's cæcum. The important feature of the colon is its relative fixidity to the pyloric sphincter and adjacent great curvature of the stomach. The position of the pyloric sphincter indicates the separation of the colon into two portions, viz. right, short, wide, proximal colon, and left distal colon. It is interesting to note the presence of a band 2–2·5 cm. broad which passes across the thickened pyloric sphincter from the right of the lesser to the right of the greater

omentum. This band, though adherent slightly to the pylorus, forms a continuity between the colon in this region and the lesser omentum. In chameleon (as a type of Reptilia) the commencement of the colon is almost brought into contact with the pylorus by a ventral fold, which, crossing the latter, becomes continuous with the ventral mesogaster at the

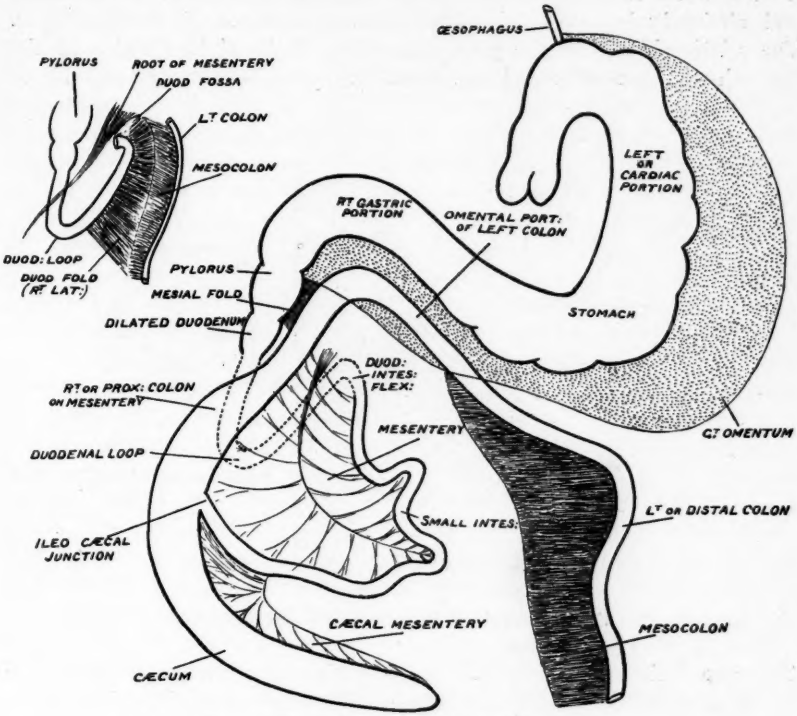

FIG. 4.—The gastro-intestinal tract of Macropus.

abdominal wall. In a bat from the middle of the fine mesial fold and from the gastro-hepatic omentum two slender membranes are given off, traceable to the ventral wall, where they meet. In a male adult kangaroo, ascending from the ileo-cæcal junction, which was close to the lower part of the duodenal loop, was 4·5 cm. of right colon. This was mobile, being swung on the common mesentery with the small gut—the distance between the two intestines being 10 cm. It lay with the mesentery ventral to the duodenal loop, off which it could be raised. It

was closely applied at the pylorus by a mesial fold—the distance between colon and sphincter being only 1·5 cm. This was followed by a comparatively fixed portion of colon (proximal portion of distal or left colon), 14 cm., really attached to the mesocolon but closely related to the great curve of the stomach, owing to the fact that it and its mesocolon have been included in the great omentum. This is in contrast to the koala, and obviously is associated with the erect attitude of the macropod. The relationship is to the great curvature of the right division of the stomach—*i.e.* non-sacculated and sacculated parts,—and never extends to

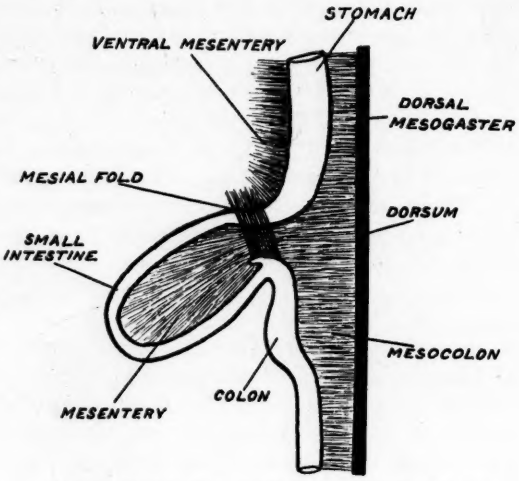

FIG. 5.—Mesial attachment in Chameleon (Reptilia).

the apex of the stomach bend. The colon is nearer the greater curvature of the stomach in wallaby than in the kangaroo, and there is a closer attachment of the colon on the right than on the left in both. In other words, the fixation of colon and mesocolon to the great omentum begins from right to left.

In the above specimen the distance between the colon and the greater curvature near the pyloric sphincter was 2 cm., on the left 7 cm., and between these points 3 cm., *i.e.* the separation of mesocolon from great omentum was gradual; but in another the distance between the two on the right was 3·5 cm. and on the left 4·5 cm., and so the separation of mesocolon from great omentum was more sudden. In a kangaroo whose cæcum was 35 cm. long and right free proximal or mesenteric colon 10 cm.

the attachment at the pylorus and the great curvature was 17 cm.; and in a wallaby whose right free colon was 10 cm. the attachment was 14 cm. We frequently see peritoneal adhesions or bands from the dextral margin of the right free colon to the descending duodenum even as far as its lower third, and in a fœtus I have seen a band connecting the right colon to the whole of the descending duodenum. Here nature gives us an indication of her method of dorsal fixation of the colon. The common mesentery, though shortened here, is not dorsally fixed, *i.e.* its base or dorsal attachment is not lengthened; and, further, the mesoduodenum is present and the duodenal loop is mobile. The left colon begins opposite the pyloric sphincter, and, as above stated, is at first attached to the great omentum (lesser sac). Leaving the great omentum on the left, it is seen to be swung freely on its mesocolon (dorsal mesentery), the greatest width of which may equal 7–12 cm. This latter is attached dorsally between the two psoas muscles and the kidneys for about 10 cm., and gradually disappears into the pelvis. The left colon measures in the kangaroo 80–100 cm., and in wallaby about 46 cm. As showing the method of inclusion of the distal colon by the great omentum, a peritoneal band may be noted passing from the left of this structure to the distal colon, where it is commencing to be swung freely on the mesocolon. The large intestine may be thus summed up:—There is a well-defined, freely mobile cæcum. This is followed by a mobile, wide, but short right or proximal colon swung on the common mesentery with the small gut. This extends as far as the pylorus, where it is closely applied; and, furthermore, it is frequently connected by a band or bands to the descending duodenum. The left or distal colon begins opposite the pyloric sphincter. At first it is related to the great curve of the stomach, being with its mesocolon included in the great omentum (lesser sac). Leaving the omentum, it is traced into the pelvis, being looped and swung freely on its mesocolon or dorsal mesentery.

(*c*) *Tasmanian Devil* (*Dasyurus sarcophilus*).—On displacing the intestinal tract and dorsal mesentery to the left, the termination of the right lateral or duodenal fold is noted at a point 10 cm. from the pylorus. This corresponds to the termination of the duodenum, and here also a well-defined independent branch of the right vagus is noted, as shown in the diagram of my previous communication. So fine may be the fold here, that it may be necessary to stretch the last 2 cm. to detect it. The base of the fold, which is well defined, runs along the mesocolon near its dorsal attachment, from the root of the mesentery above, disappearing into the pelvis below. If the duodenum were looped this fold would form part of the boundary of a primary duodenal fossa. There is

no mesial fold bringing the colon into relation with the pyloric region—the minimum interval in an adult being about 18 cm.

(*d*) *Australian Opossum* (*Trichosurus and Pseudochirus*).—1. *Trichosurus.*—A reference to my previous diagram (*Journal of Anatomy*, 1916, vol. li. p. 8) of Trichosurus shows, as in koala, a well-defined duodenal loop formed by a descending limb (10 cm.) and an ascending shorter one (4 cm.). The loop is mobile, there being a free mesoduodenum present. From the ascending limb is a well-defined right lateral or duodenal fold, transverse above and traceable to the mesocolon of the distal colon, and oblique below, being prolonged dorsally by the side of the attachment of the mesocolon into the pelvis, where in the female it may become continuous with the right broad ligament. The greatest width of the fold is 2·5 cm. Between the upper part of the fold—the root of the mesentery—and duodeno-intestinal flexure lies the primary duodenal fossa. As in koala, we have relatively a large cæcum (45–55 cm.) and right or proximal colon (25 cm.) swung with the small intestine on the common mesentery; and a left or distal colon (90 cm.) swung freely on its own dorsal mesentery (mesocolon), which is traced along the dorsal wall between the two psoas muscles for 7 cm. The colon is not, however, as in koala, closely attached to the pyloric region As the right colon, after crossing with the common mesentery the lower third of the descending limb of the duodenum, approaches the root of the mesentery, it narrows and becomes closely bound down for a limited extent of about 1 cm. to the mesoduodenum and pancreas; but in addition, for 3 cm. before the "fixed" area is reached the right colon may, as in the Platypus, be related by peritoneal adhesions to the descending duodenum and the mesoduodenum. Occasionally a fine process (mesial) may be traced from the "fixed" colon (corresponding to the separation of right from left colon) to the pyloric region across the pancreas—the distance between the two being about 3 cm. in an adult.

2. *Pseudochirus.*—Here the duodenal loop is not so mobile as in Trichosurus, nor is the right lateral fold so well developed. There is a relatively large cæcum (33 cm.) in contrast to the narrow large intestine. The right proximal colon for the first 6 cm. is swung freely with the cæcum and small intestine on the common mesentery. It crosses the lower part of the descending pole of the duodenum, and ascends more or less parallel to it—there being only an interval of about 1·25 cm.—till the commencement of the duodenum is reached. Peritoneal adhesions are noted connecting this portion of the colon and its mesentery to the duodenum and mesoduodenum. The left or distal colon measures 54 cm., and at first (8–10 cm.) comes into relation with the lesser sac, being included by the great omentum.

This portion forms an arch from right to left, following practically the great curve of stomach as far as the extremity of the right process of spleen. It is then continued into the pelvis, being swung freely on mesocolon off which the great omentum gradually recedes. As regards the fixation of colon, it is important to note that Pseudochirus approaches more closely the human type than Trichosurus.

(*e*) *American Opossum* (*Didelphys marsupialis*).—In this Marsupial the peritoneal arrangement is less specialised than in Platypus, although the

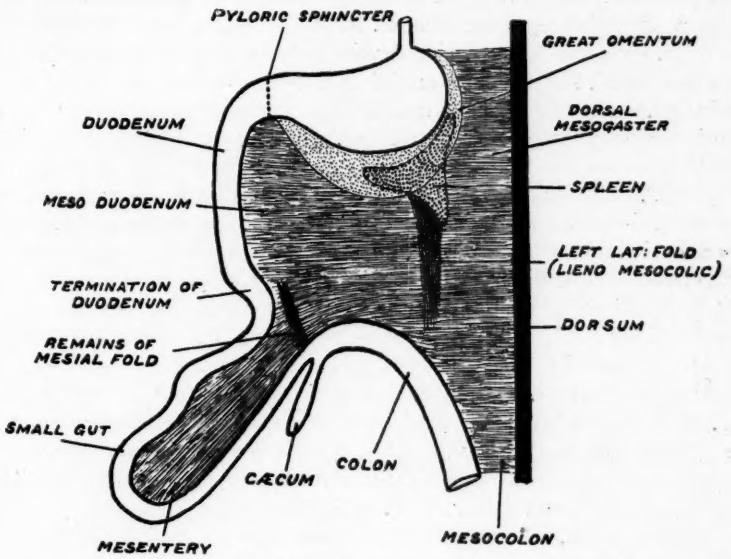

FIG. 6.—Intestinal plan of American Opossum (*Didelphys marsupialis*).

stomach is more mammalian than that in Monotreme (see fig. 6). There is no approximation of the colon to the pyloric region—3 cm. intervening,—but a mesial fold is seen extending from the former to the mesoduodenum about the termination of the duodenum level. There is a descending duodenum with a "tucking in" at its termination. In some specimens this latter may be so developed as to produce a duodenal loop, but we never have the duodenal development seen in Monotremes or Australian Phalangers. From the dorsal aspect of the "tucked-in" part is a small band, 1 cm. long and ·5 cm. wide—right lateral or duodenal,—passing to the right aspect of the dorsal mesentery of the colon; and the earliest trace of a duodenal fossa is seen between it, the intestine, and the

mesentery. If we divide or stretch the mesial and duodenal folds we can produce what corresponds to a simple reptilian condition (*e.g.* Agama) of an intestinal loop swung on a dorsal mesentery. There is a great omentum supporting the body and right process of spleen, while the left process is suspended on the lieno-mesocolic (left lateral) fold. This is free from the kidney. The tubular cæcum may be only 3 cm. long, and usually there is not more than 1 cm. of colon proximal to the mesial fold, *i.e.* swung on the mesentery of the small intestine. As in the Tasmanian Devil, we have a short primitive colon swung on its dorsal mesentery (mesocolon).

In a Virginian opossum (32 cm. snout to vent) the short wide cæcum was 5 cm. long, but there was no development of colon on the mesentery of the small gut, *i.e.* to right of mesial fold, which terminated on the meso-duodenum. The commencement of the colon was not approximated to the pyloric region, about 3 cm. intervening. There was marked inequality of growth between the mesoduodenum (3 cm. wide) and mesentery of small gut (8 cm.). The duodenum was better defined than in the preceding, and the "tucked-in" termination formed a small though decided loop. There was a duodenal band (·75 cm. long and ·3 cm. wide) from the duodenal loop to the mesocolon of the colon, and a duodenal fossa was present.

(*f*) *Bandicoot* (*Peramelidæ*).—In this Marsupial the intestine is less specialised than in either of the Monotremes (fig. 7). There is no defined duodenal loop, and the arrangement of the small gut resembles that of the carnivorous dasyures. In a specimen kindly given to me by Professor J. P. Hill the duodenum was defined as a portion extending 2·5 cm. from the pylorus, whose dorsal mesentery or mesoduodenum was narrowed—inequality of growth—compared with that beyond it. The greatest width of this mesoduodenum was 1·75 cm., while that of dorsal mesentery of small gut reached 7 cm. Apart, however, from this shortened mesentery we have, defining the termination of duodenal portion, a band—right lateral or duodenal—about 5 cm. long and passing dorsal to the mesentery of the small gut. This was narrow above at its attachment to the mesenteric edge of the duodenal termination, but broadening below at its attachment to the right aspect of the mesocolon, and finally became continuous, ventral to the colon before it enters the pelvis, with the left lateral or lieno-meso-colic fold. The result is that a pouch is formed between the ventral aspect of the gut and the junction of the two folds, which is traceable into the pelvis. The large intestine was swung on the mesocolon, *i.e.* was all primitive distal or left colon, there being no development on the common mesentery of the right, proximal, or mesenteric colon. At the commencement of the colon a curved cæcum was noted (5 cm.) connected to the termination of the small intestine. The distance between

the pylorus and the ileo-colic junction, which were practically in the same mesial plane, was about 5 cm. At the latter a mesial band was seen, traceable only as far as the root of the mesentery and not to the pyloric region. The body (3 cm.) and large right process (5 cm.) of spleen are suspended on the great omentum, while connected to the small left process (1·25 cm.) and great omentum is the left lateral fold (lieno-mesocolic). Below, this is related at first to the left aspect of mesocolon, but more caudally to the dorsal wall between the dorsal attachment of the meso-

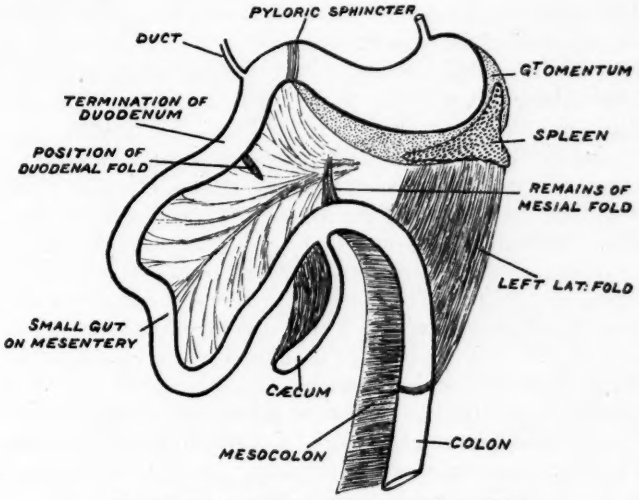

FIG. 7.—Gastro-intestine of Bandicoot (Peramelidæ).

colon and the left kidney. Its left margin is free, and measures 4 cm. The fold, with the pancreas it supports, is free from the dorsal wall and left kidney. Just above the level of the fundus of the bladder it is continuous, as stated, with the duodenal fold ventral to the colon.

GENERALISATIONS.

Owing to the diversity of intestinal types met with in the two orders Monotremata and Marsupialia, light is thrown on the method of fixation of the mammalian gut and the significance of bands in connection with the human intestine.

1. *Duodenal (Right Lateral) Fold.*—The definition of the mesoduodenum is a result of inequality of growth between it and the common mesentery,

dependent primarily, however, on the functional activity of the duodenum. The duodeno-intestinal junction corresponds to the termination of a direct branch of the right vagus, as is well seen in the Tasmanian Devil. The duodenal fold can only be regarded as a secondary or adhesion fold (zygosis) —a view held by Moynihan. An early stage of its development is seen in Didelphys, while its maximum development is seen in Trichosurus and the kangaroo. The disappearance of both the fold and fossa is associated with dorsal fixation of duodenal loop and pancreas, as is shown in Echidna and occasionally in the wombat. The duodenal fossa described in the above orders is the primary duodenal fossa, and is met with as such throughout the Mammalia up to Anthropoids.

2. The *left lateral* (*lieno-mesocolic*) *fold* as a factor in approximating spleen, colon, pancreas, and left kidney has been previously dealt with in detail.

3. *Mesial Fold.*—From the above studies the proximity of colon to pyloric region is seen to have "selection" value, being associated with development of the proximal colon—the part situated on the common mesentery. Absence of this proximity, with non-development of the mesial support, is associated with non-development of the right or proximal colon. The two extremes in Marsupialia are met with in the koala and carnivorous dasyures. Intermediate grades are met with in Peramelidæ and Didelphydiæ. The right colon—like the mesial hepatic lobe—might be regarded as a new or "experimental" colon. Here we find large and small cæca, appendices, coils and loops. The somewhat complicated right colon of rodents is simplified in Lemuroidea, and the human type appears in the Platyrrhines. In the Tasmanian Devil a well-defined direct branch of the right vagus is traced to the commencement of the colon (left, primitive, or mesocolic), so that development of the proximal or mesenteric colon is dextral not only to the mesial attachment but to the "vagal" area. It is interesting to note, as seen in Lemuroidea, Platyrrhines, Catarrhines, and great Anthropoids, that fixation of the right colon, *i.e.* shortening and dorsal fixation of its common mesentery, takes place from above downwards, *i.e.* begins at the mesial attachment. In the wombat the dorsal fixation of ileo-cæcal region is associated with a free right colon. From the mesial fold also begins the attachment of distal colon and mesocolon to great omentum, as evidenced in Macropus, and which extends in higher mammals to the spleen. Fixation of the "descending" colon follows fixation of the "splenic" flexure, proceeding from above downwards.

SOME NEW POINTS IN THE ANATOMY OF THE NASAL SEPTUM, AND THEIR SURGICAL SIGNIFICANCE.

By J. L. AYMARD, Captain R.A.M.C. (Temp.), Cambridge Hospital, Aldershot.

IN recent years more particularly, the progress of the anatomy of a part appears to advance concurrently with its surgical or medical importance, and the anatomy of the nasal cavities is no exception.

The existence of two distinct movable joints in the septum does not appear to have been recognised as such, and the distribution of the perichondrium cannot be said to have been either described by the anatomist or understood by the surgeon.

The presence of a permanent vascular arrangement within the septal cartilage has apparently also been overlooked.

The septal cartilage is usually represented as being a perpendicular plate attached behind, below, and above, and is illustrated as presenting a free border, covered only by the soft parts extending from the anterior border of the nasal bones forwards and downwards, and embedded between the median borders of the lateral cartilages. In the first place, exception must be taken to the designation of the upper lateral cartilages. They never exist as separate cartilages, neither are they separable except by force from the rest of the septal cartilage. Would it not be far more correct to describe each so-called lateral cartilage as the lamina triangularis, and the vertical cartilage as the lamina perpendicularis of one large cartilage, say the cartilago nasalis major? Professor Macalister has already described them as the "lateral expansions of the septal cartilage."

CARTILAGO NASALIS MAJOR.

For practical purposes it would be much better to designate landmarks indicating the general position and extent of these cartilages, rather than give dimensions which vary so considerably in each individual case.

The lamina perpendicularis (L.P., fig. 1) of this cartilage presents four distinct borders.

The posterior border is firmly attached to the anterior edge of the lamina perpendicularis ethmoidalis (L.P.E.), the perichondrium of the former

being directly continuous with the periosteum covering the latter, thus forming a strong ligamentous band.

The superior border between i. and ii., fig. 1, and A, fig. 2, is flattened and grooved to receive the prominence caused by the median junction at the under surface of the nasal bones; the groove is continued forwards, where it widens out to form the lamina triangularis (L.T., figs. 1 and 2) or so-called lateral cartilages. This plate L.T. is triangular in shape, its base being attached to the anterior edges of the nasal bones and its apex

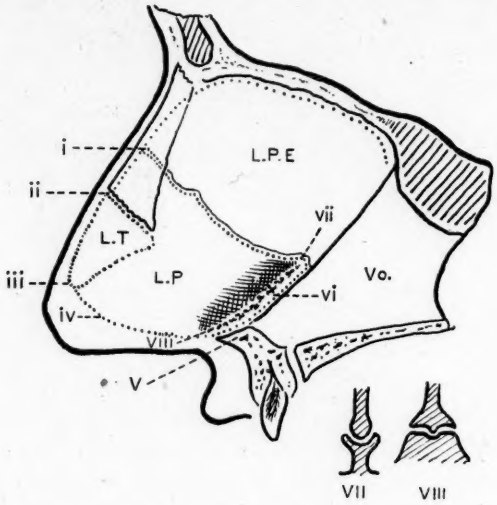

FIG. 1.—Septum of the nose showing the relationships of the septal cartilage. VII., section across chondro-vomeral joint; VIII., section across chondro-maxillary joint.

(fig. 1, iii.) extending to the superior angle of the anterior free border. In flat noses the lamina triangularis takes a gentle curve, and in sharp narrow ones a shape corresponding.

The anterior border (fig. 1, iv.) is free and rounded, and can be readily seen through its coverings when the columna is held aside.

The inferior border is pear-shaped in section (fig. 1, vi.; also fig. 2, C) and more oval (fig. 1, vii., and fig. 2, B). Where it forms the chondro-maxillary joint with the crista incisiva (fig. 1, v., and fig. 2, D) it is flattened and terminates in an obtuse angle.

Surface markings for localising the posterior border of the lamina perpendicularis.—The posterior border of this lamina lies a third of

an inch behind the anterior edge of the nasal bones, from which it slopes irregularly downwards and backwards.

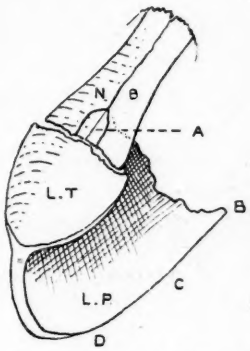

FIG. 2.—The parts of the septal cartilage. (For explanation see text.)

FIG. 3.—The parts of the septal cartilage as described in accepted works.

A, B, C, D, sections across the margin of the septal cartilage at the points indicated in fig. 2 by corresponding letters.

THE CHONDRO-VOMERAL AND CHONDRO-MAXILLARY JOINTS.

The descriptions given in the leading works of anatomy merely state that the rounded end of the septal cartilage is received into the groove upon the anterior superior edge of the vomer and maxilla. This is correct as far as it goes, but at the same time they offer no proofs that this is not a mere osteo-cartilaginous junction.

The movement permissible at the lower septal joints forms a complete semicircle limited to a right angle each side of the perpendicular.

This, I think, is the only joint in the body permitting such extensive movements, and it appears to be constructed for the purpose. Further, it is, I believe, the only freely movable joint entirely composed of cartilage on the one hand, and a non-cartilage-covered bone on the other. A study of the joint demonstrates the fact that pressure upon the anterior superior surface of the septal cartilage causes it to bend in the direction of its long axis. Pressure upon the anterior inferior border causes the cartilage to bend obliquely upon itself, with a certain amount of transverse movement across the chondro-maxillary joint, combined with the lateral movement described.

Were it not for this joint, fractures and dislocations of the cartilage would obviously be far more frequent than they are. There would be no object in a joint of a similar description with the ethmoid plate, therefore it does not exist.

The chondro-vomeral joint (figs. 4 and 5), as I prefer to term it, is in every sense of the word a very perfect joint constructed for a definite object. The perichondrium and periosteum are in a sense continuous, but there is much more than this to be noted.

In the first place, whatever the condition of the vomeral groove may be —that is to say, though the edges may be irregular or even absent here and there,—the pear-shaped lower portion of the cartilage remains fairly constant and the capsular attachments likewise. The definite object of this

Fig. 4. Fig. 5. Fig. 6. Fig. 7.

FIG. 4.—Transverse section of chondro-vomeral joint, with covering membranes removed.
FIG. 5.—Showing the disposition of perichondrium and periosteum at chondro-vomeral joint.
FIG. 6.—The same joint showing included fat and the covering of mucous membrane on one side.
FIG. 7.—The articulating surfaces of the chondro-maxillary joint.

joint is without doubt to allow of free lateral movement when from any cause pressure is applied from above.

A concussion plate is also provided in the shape of a layer of fat (fig. 7) between the periosteal perichondrial layers. The amount of movement possible, owing to the loose attachment of the perichondrium and periosteum, accounts for the fact that in a deviated septum the articular portion of the cartilage may easily occupy a transverse position across the groove (fig. 10), forming a projection not infrequently mistaken for a crest.

The chondro-maxillary joint.—The portion of the inferior border of the septal cartilage entering into the formation of this joint is usually represented by the anterior third. The cartilage is flattened and pointed (fig. 7) to rest upon the corresponding junction of the maxillary bones known as the crista incisiva. If this crest is rounded or otherwise shaped the cartilage takes a corresponding form. The corresponding coverings are similar to those of the chondro-vomeral joint, but much tougher, thicker and looser.

The apparent object here is to allow lateral rotation as well as a diagonal lock-gate motion.

The surgical importance of the above is that a blow directed upon the anterior edge of the cartilage bends it vertically upon itself, allowing a position to be taken diagonal to the crista incisiva and thus avoiding fracture. Another point is that, unless the membranous disposition and its nature in this area of the septum is thoroughly understood, the surgeon will find himself in difficulties.

The structures referred to should always be divided carefully with a blunt-pointed bistoury.

The Immediate Joint Coverings.

It is generally taught that the perichondrium covering the cartilage and the periosteum covering the vomer are continuous and attached along the crest. Only to a certain extent is this correct. The perichondrial arrangement is somewhat complex.

In the first place, careful investigation shows that the perichondrium does not, as the usual description implies, merely merge into the periosteum. Below the orifices of the chondro-vascular system (fig. 1, vi.) the perichondrium is continued loosely around the cartilage, and is continuous with the perichondrium of the opposite surface (fig. 5).

The periosteum (fig. 9), on the other hand, instead of being continuous with the perichondrium, as generally described, merely sends a process upwards to be attached to the perichondrium below the vascular openings, thus loosely covering the vomeral trough (sulcus vomeralis). The perichondrium in a similar manner sends a process downwards to join the periosteum, thus forming a joint ligament.

The Surgical Significance of the Points referred to.

The anatomy of the septal cartilage is principally interesting from the point of view of its partial removal, and here I must protest against the teachings in our leading text-books. Most nasal surgeons will agree with me that at least 75 per cent. of the cases presenting themselves for obstruction require the removal of only a moderate amount of cartilage and bone. The illustrations referred to advise an eighth of an inch of the anterior pillar of the septum to be left, whereas no experienced surgeon would think of leaving less than a quarter of an inch as a general rule. Further, the removal of the foundation of even this support by chiselling the maxillary crest is recommended freely without reserve and without any warning as to possible ultimate cosmetic effects. In the above case, we

should teach the student not to remove a given area, but only just so much cartilage or bone as will give the necessary space for free passage of air or any other purpose.

Most surgeons use Ballenger's knife to remove cartilage, an ingenious but by no means ideal instrument. The usual procedure is to pass the knife along the upper edge of the area to be removed, down the back, and along the lower border. A reference to figs. 10 and 11 shows the difficulty (with the cartilage lying over, and particularly with three sides cut through) of cutting the cartilage close to the bone—since any downward pressure of the knife only further depresses the free cartilage. The point to remember is, that the piece of cartilage is left possibly lying across the vomer. It being mechanically impossible to remove this portion of the cartilage with Ballenger's knife unless the sides of sulcus vomeralis are absent, I prefer to cut flat the front, top, and back, and then remove the lower margin with a small trough-shaped gouge, having, if necessary, first divided the perichondrium with a blunt bistoury.

I would draw attention to the fact that the vascular system extends to the inferior angle of the antero-inferior margin of the cartilage, and that this blood-supply is not likely to be re-established if once cut off, which is of importance with reference to the pillar of support proposed to be left.

The Septal Coverings.

The perichondrium is very firmly attached to both surfaces of the cartilage, whereas the periosteum is only loosely attached to the bone and readily removed.

This attachment is marked everywhere except within the joint, and is due to the perichondrial processes which extend deep into the cartilage, so that when the membrane is removed these processes are for the most part torn and remain behind.

The periosteum and perichondrium are about equally adherent to the mucous membrane. Over the chondro-ethmoidal junction there is no special attachment, the one membrane merging into the other. Although the perichondrium is described as being divisible into many layers by mechanical means, I have been able to separate two layers.

The mucous membrane covering the septum has been fully described in standard works. I recognise three layers—a superficial, a middle, and an inner layer; between the two latter run the large vessels and nerves. The mucous membrane is closely attached to the perichondrium and periosteum except over the anterior third of the cartilage. In this position the membrane is very loosely attached. This fact should be noted, because

it is entirely due to this loose condition in this region that failure so often takes place.

The usual incision for resection is made the full length required at the start, and cuts down to the cartilage, severing the perichondrium. The difficulty of endeavouring to separate the (in this region) tough mucous membrane from the closely attached perichondrium is the cause of operative trouble.

It is far better not to incise the perichondrium at first and only to make a sufficient cut to allow the introduction of the elevator used on Watkins Williams' principle. The incision can be enlarged to the full length when the membrane around is free for a good start.

Experts teach that the cartilage be now cut through and the elevator passed in between the same and the perichondrium and raised to the full extent. As a matter of fact, I think this procedure is more apt to take place by accident than design.

I would draw the attention of students to some other special points of importance. In the first place, all serious hæmorrhage can be avoided when operating if the positions of the larger trunks of vessels are remembered.

Just inside the anterior choana, behind its lower internal border, the palatine arteries must be carefully noted, especially when preparing to remove a portion of the crest.

The next group of vessels likely to be injured are those coursing along the vomer in the mucous membrane and in the region of its crest.

Should the mucous membrane be separated into layers (a not uncommon occurrence), it follows that in using the punch forceps these vessels are very likely to be divided between the bone and the punch. The palatine nerve may also be destroyed in a similar manner, thus leading to subsequent trophic changes in the mucous membrane.

The Significance of the Perichondrial Attachment in relation to the Operation of Sub-Mucous Resection.

In all the leading works upon this subject, this operation is *primarily* described as a muco-perichondrial detachment. I say primarily, because in one illustration the sub-mucous resection is referred to, and upon the same page it is described as muco-perichondrial, thus greatly confusing the student. It is clearly wrong to describe the operation as a sub-mucous perichondrial one. The illustrations upon this subject show quite correctly the mucous membrane loosely separated outside the speculum, whereas a sub-muco-perichondrium could not be so illustrated.

It is better to imagine the cartilage of the septum to be suspended in a covering (fig. 5), completely enclosed in front and only opening behind at the ethmoid margin, where it is anatomically continuous with its periosteum.

If this fact be grasped, it will be at once seen that any elevator once entering beneath this covering has no chance of exit except by force.

An elevator passed between the perichondrium and the cartilage and pressed downwards will find its way into the joint round the cartilage and up the opposite side. This fact can be readily proved by experiments.

The perichondrium itself is capable of being split into at least two different layers. Upon the lateral surface of the cartilage it is very firmly attached, and less so to the mucous membrane; but, once it reaches around the articular surface below the edge of the osseous groove, it is only loosely attached. The real periosteum rolls loosely over this bony edge, where it lines the bony trough (the sulcus vomeralis) and joins the opposite layer. If the cartilage is pushed well over to either side, the condition of the attachment, at one time loose and another time tight, is readily seen. A layer of fat is met with between the perichondrium and periosteum, and also between the periosteum and floor of the vomeral groove.

If the cartilage removed from a recent septum be examined it will appear to be destitute of covering, but an incision into it and firm pressure with an elevator will reveal the perichondrium intact. In some instances the perichondrium may be found to have been removed for a short distance on the proximal side of the cartilage, but seldom, if ever, on the distal one.

I am not advocating any attempt to remove the perichondrium intact. I think it is very questionable whether two intact surfaces of perichondrium left behind would serve any useful purpose, much less if they were in a bruised and torn condition.

The Membranous Folds of the Chondro-Vomeral Joint.

When passing the elevator downwards, it is a golden rule, upon approaching the joint, to stretch the parts well outwards, or, where considerable deformity exists, to cut the membrane *from behind forwards and towards the cartilage* with a curved blunt-ended bistoury. In most cases, if the elevator is pressed firmly outwards at this point and force used, the attachments will give way and the elevator pass downwards between the bone and the periosteum.

It must be remembered that, if the cartilage is (for example) leaning over to the left, the attachments on this side will be loose, and it is

quite easy to force the elevator, membrane and all, into the joint. It is a good plan, therefore, when dividing the same with a bistoury, to press the cartilage well over to the opposite side to that on which the incision will be made, for by so doing the membranes attached are put upon the stretch.

The membranous folds of the chondro-maxillary joint are for all

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 11.

Fig. 12.

Fig. 13.

Fig. 14.

Fig. 15.

Fig. 8.—Section of chondro-maxillary joint showing the arrangement of the perichondrium and periosteum.

Fig. 9.—Another diagrammatic section showing the included layer of fat, the capsule and mucous membrane (on one side).

Fig. 10.—Dislocation of septal cartilage presenting a condition frequently mistaken for a spur of bone.

Figs. 11, 12, 13, 14.—Types of dislocation at the chondro-vomeral joint.

Fig. 15.—Type of chondro-maxillary displacements.

practical purposes similar, but (as before described) thicker, looser, and tougher.

Fractures and Dislocations of the Septal Cartilage.

Although acute conditions of the above are frequently referred to in the text-books, their nature is seldom defined, for very obvious reasons, whereas the chronic conditions of luxation and dislocation are extensively dealt with. Fig. 10 is by no means an uncommon condition; fig. 11 is rare; while fig. 12 shows a direct dislocation either side of the sulcus vomeralis. I have never seen such a dislocation. The loose condition of the joint coverings allows for extensive displacement, but long before

this direct lateral dislocation could take place the cartilage would probably double up. Further, unless the nose be crushed in or the cartilage be torn from the under surface of the nasal bones and the whole margin of the ethmoidal, any sudden dislocation is a mechanical improbability. In figs. 13 and 14 we notice quite common forms due to the absence of the rim of the sulcus. Fig. 15 is not an uncommon form. The main portion of the cartilage is retained in the vomeral joint, but that over the crista incisiva is dislocated diagonally.

With regard to fractures, I am far more inclined to look to the upper and posterior borders for possible trouble, because they are not provided with movable joints. Sufficient force applied to the anterior portion of the nose must do one of two things—either fracture and dislocate the nasal bones, or depress, dislocate, and tear the upper grooved edge of the cartilage from the under surface of the nasal bones, and in this case it will probably break it off from the lamina ethmoidalis perpendicularis, and thereby deflect the anterior aspect of the nose. In this way only can I account for the fact of a crooked nose without displacement of the nasal bones after an accident.

The Chondro-Vascular System.

Situated in an irregular line (fig. 1, vii.) will be seen the orifices and branching of the canals forming this complete system. These canals occupy the whole area described as the pear-shaped lower border, and also the portion anterior to this. They contain blood-vessels which arise from the mucous membrane and penetrate the perichondrium. These canals do not in any case communicate with each other, the vessels entering and returning by the same orifice. This vascular system is best studied and demonstrated in the septal cartilage of the sheep, when the septum, devoid of perichondrium, has become nearly dry. It may be beautifully seen by holding the cartilage before a strong light against a bright white background. In well-developed fresh human subjects the same arrangement can easily be recognised. These vascular canals are very characteristic and distinctive; they never anastomose, they present rounded ends, and seldom, when branched, project beyond the centre of the cartilage. Upon the other hand, single straight canals can frequently be seen passing across the upper portions of the cartilage.

Since writing this article my work as a plastic surgeon at the Cambridge Hospital, Aldershot, has given me an unique opportunity of examining a large number of costal cartilages, and I have no hesitation in saying that they possess a vascular system precisely similar to that described above in

the septal cartilage. The system is very plain to the naked eye, and can be easily traced by the presence of blood. I therefore venture to disagree with those anatomists who describe such a condition as mere prolongations of persistent perichondral processes. The only difference I have so far been able to find between the vascular canals in fœtal cartilage and the vascular canals in the permanent cartilages referred to, is that in the former the ends of the canals are more pointed and branched, whilst in the latter they are rounded. Injections of these canals produce very interesting conditions, but their description I must leave to another occasion.

Surgical Importance.

If the coverings of the cartilage are removed upon both sides at the chrondo-maxillary joint, the complete internal blood-supply of this thickened piece of cartilage will be found destroyed, a fact which leads to the question as to what eventually becomes of this pillar base which is left by the surgeon for cosmetic purposes.

I have very great pleasure in acknowledging valuable assistance from Professor Wood Jones, who very kindly prepared illustrations from my rough drawing, and from Dr Watkins Pitchford of the South African Institute for Medical Research, Johannesburg.

A SUBJECT WITH COMPLETE TRANSPOSITION OF VISCERA.

By M. Amin Abdel Rahman, *Assistant Professor of Anatomy, Cairo.*

The body was that of a typical old Egyptian male, between 85 and 90 years of age, very well developed, and without any external signs of disease. On opening the body on its ventral aspect we found the following conditions:—

1. *Thorax.*

(*a*) Right subclavian vein and right jugular united to form the right innominate, which was found passing downwards and to the left to meet the left innominate on the left side of the ascending aorta, to form the superior vena cava. As the right innominate vein passed to the left it crossed the arch of the aorta with the commencement of the subclavian, carotid, and innominate arteries, in that order from right to left.

(*b*) *Heart.*—On opening the pericardium, the heart was found lying in position with its apex pointing downwards, forwards, and to the right, instead of to the left. From the base of the heart the vessels were found arising in the following order:—

Pulmonary artery.—Arising from the left ventricular chamber, then going upwards and to the right, where it was found bifurcating under the arch of the aorta.

Aorta.—Arising from the right ventricular chamber and going upwards and slightly to the left, this was then directed upwards, backwards, and to the right in an arched manner, becoming continuous with the descending thoracic aorta that was found lying on the right side of the vertebral column. The vessels arising from the convexity of the arch were found, as already mentioned, to be, from right to left, the right subclavian, right carotid, and innominate; this last bifurcated at the left side of the root of the neck into left carotid and subclavian. The right vagus was found crossing the arch superficially, and giving in its concavity its recurrent branch, which looped below the arch and then went upwards to the right side of the larynx.

The auricle situated on the left side of the heart received from above the superior vena cava and from below the inferior vena cava. Its

appendix was seen to a great extent from the front, overlapping the origins of the two great arteries.

The vena azygos major arched over the root of the left lung and opened into the superior vena cava.

The ventricle of the left side was found to have a very much thinner wall than the corresponding right chamber; it gave origin to the pulmonary artery, and communicated with its auricle by the tricuspid opening. This chamber occupied more than half of the anterior surface of the heart.

The ventricle on the right side had much thicker walls, about 23 mm. thick. It gave origin to the aorta, and communicated with its auricle by the mitral opening. This chamber occupied less than half of the anterior surface of the heart.

The auricle on the right side received the four pulmonary veins, coming from both lungs. Its appendix was hardly seen from the front of the heart.

(*c*) *Lungs.*—It was difficult to find the three fissures in either the right or left lung, but the left one was shorter and broader than the right.

(*d*) The *descending aorta* passed down on the right of the vertebral column and œsophagus, behind the root of the right lung and pericardium.

2. *Abdomen.*

The *liver* was found lying with its larger lobe and gall-bladder on the left side of the body, while the smaller lobe was on the right. The notch on the posterior surface for the œsophagus was to the right side of the middle line of the body, while that for the inferior vena cava was on the left. The round ligament passed towards the left from the navel, and disappeared in the fissure between the two lobes (fig. 1 : 5).

Stomach.—The cardiac opening, fundus, and body were found lying in the right side of the abdomen; the pylorus, directed to the left, lay under the large lobe of the liver. The lesser curvature was directed from right to left and downwards, as was also the great curvature.

The *spleen* was found lying behind and to the right side of the fundus of the stomach, in the right hypochondriac region (fig. 1 : 8).

Duodenum.—Began at the pylorus on the left side of the abdomen, and had the convexity of the second portion directed to the left. Its third part passed from left to right, crossing first the inferior vena cava and then the aorta, and ended on the right at the level of the 2nd lumbar vertebra, where it became continuous with the jejunum.

The *pancreas* had its head directed to the left, lying in the concavity

of the duodenum, whilst its tail lay on the right side, abutting against the hilum of the spleen.

The *cæcum and appendix* were found in the left iliac fossa, with the appendix hanging into the cavity of the true pelvis (fig. 1: 13, 14).

FIG. 1.—From a photograph of the case here described.

1, aorta; 2, superior vena cava; 3, "left" lobe of liver; 4, "right" lobe; 5, round ligament; 6, cardiac part of stomach; 7, pyloric part; 8, spleen; 9, tail of pancreas; 10, inferior mesenteric vein; 11, superior mesenteric vessels; 12, inferior vena cava; 13, cæcum; 14, appendix; 15, pelvic colon.

Colon.—The ascending part lay in the left side of the abdomen. The transverse colon began on the left, under the larger lobe of the liver, and ended on the right, under the spleen; from this the descending colon passed down on the right side of the abdomen to be continuous with the pelvic colon (fig. 1: 15).

The *kidneys* were both on the same level.

The *aorta* descended slightly to the right of the middle line and bi-

furcated into the common iliac arteries at the level of the 4th lumbar vertebra. Its branches:—

The gastric artery passed to the right and, after reaching the cardiac end of the stomach, followed the small curvature.

The splenic artery was directed to the right, ending in the hilum of the spleen.

The superior mesenteric artery passed downwards, forming a curve with its concavity to the left. The inferior mesenteric artery, taking origin from the right side of the aorta, crossed the right common iliac to become continuous with the superior hæmorrhoidal artery.

Inferior vena cava.—Formed on the left side of the body of the 5th lumbar vertebra by union of the two common iliac veins, the right vein crossing to the left. It then ascended on the left of the aorta, passing behind the third and second portions of duodenum and liver, to end in the left auricle after piercing the left side of the central tendon of the diaphragm.

The left spermatic vein ended in the left side of the vena cava itself, while the right vein ended in the right renal vein.

The right renal vein crossed superficial to the aorta to reach the vena cava, so was longer than the left.

The *inferior mesenteric vein* was found ascending on the right side of the abdomen and then crossing to the left at the level of the hilum of the right kidney, then crossing behind duodeno-jejunal flexure, passing superficial to the superior mesenteric artery, and then terminating in the superior mesenteric vein near its junction with the splenic.

The *superior mesenteric vein* was found on the left side of the corresponding artery, ascending to join the splenic vein, thus forming the portal vein on the left side of the middle line.

Mesentery proper.—The attached border of this was found fixed above to the right side of the body of the 2nd lumbar vertebra; it then passed downwards and to the left, ending in the region of the cæcum in the left iliac fossa.

The specimen was kept and preserved in gelatin jelly, after being injected in the usual manner with formalin solution.

NOTE ON LENGTH OF VERMIFORM PROCESS IN 220 CONSECUTIVE POST-MORTEM EXAMINATIONS.

By S. RUTHERFORD MACPHAIL, M.D., *Derby Mental Hospital.*

THE following summary is based on the result of the examination of the vermiform process in 220 consecutive "sections," viz. 115 males and 105 females, in a period of four years. All the cases were adults—the youngest being 20, and the oldest 92 years; they are classified into those under 50 and those over 50 in each sex. The shortest appendix examined was 25 mm. (1 inch), the longest 187·5 mm. (7½ inches).

220 examinations gave an average length of 99·2 mm. (3·97 inches).

115 males, average length 102·2 mm. (4·09 inches).
105 females, average length 96·2 mm. (3·85 inches).

62 males under 50, average length 104·2 mm. (4·17 inches).
53 males over 50, average length 100·5 mm. (4·02 inches).

45 females under 50, average length 95·2 mm. (3·81 inches).
60 females over 50, average length 97 mm. (3·88 inches).

The average length was therefore slightly greater in males than in females. While there was not much difference in cases over 50 and cases under 50, the average for males under 50 was slightly greater than for those over 50, while the opposite was the case among females.